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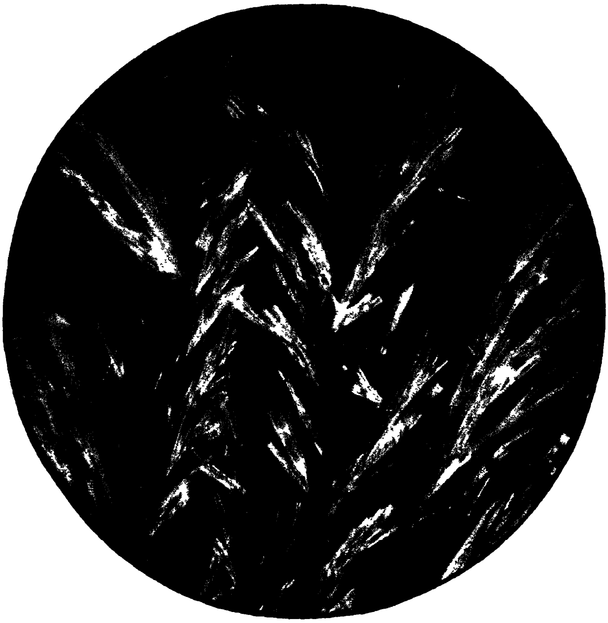
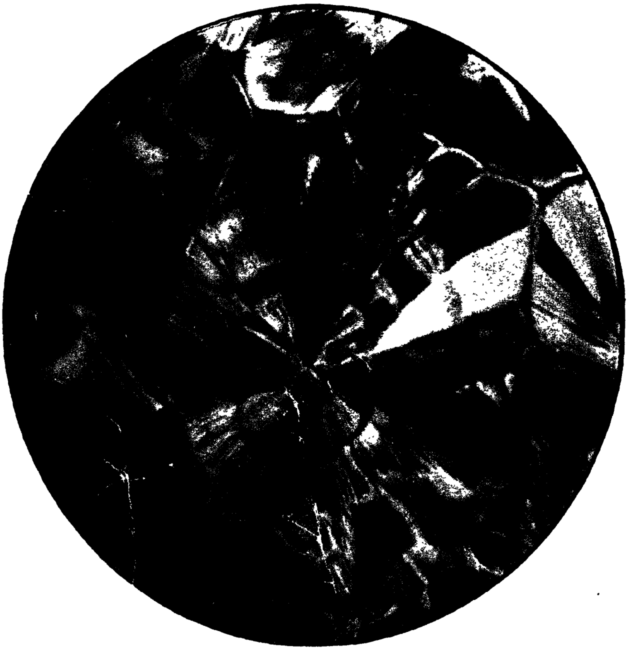


Salicin. Orthorhombic crystals from alcoholic solution.



Cocaine hydrochloride. Aggregates from aqueous solution.

CRYSTALS IN POLARIZED LIGHT (Crossed nicols).

PHARMACOGNOSY

BY

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Member U. S. Pharmacopœia Revision Committee

SECOND EDITION, THOROUGHLY REVISED
WITH 372 ILLUSTRATIONS AND 3 COLORED PLATES

LEA & FEBIGER
PHILADELPHIA

Frank T. Maher, Assistant Professor of Pharmacology in the University of Illinois, College of Pharmacy, who prepared the section on Endocrines and Hormones; to Professor Paul D. Carpenter, Assistant Professor of Zoology and Botany in the University of Illinois, College of Pharmacy, who contributed line drawings and photographs; and to Dr. Edward P. Claus, formerly Assistant Professor of Botany and Pharmacognosy, in the University of Illinois, College of Pharmacy, who prepared the section on Allergens.

E. N. G.
E. H. W.

CHICAGO, ILL

PREFACE TO FIRST EDITION

THE authors have undertaken the preparation of a new text in pharmacognosy based on the third edition of Kraemer's Pharmacognosy. This new text particularly presents the recent researches on the chemistry of drugs, and therefore it supplies a balanced pharmacognosy text and one conforming to the most modern ideas in this science; it also conforms to the standards of the eleventh revision of the U. S. Pharmacopœia and the sixth edition of the National Formulary.

The progress of pharmacognostical research in Europe during the past several decades is especially noteworthy as regards the isolation of the chemical constituents of drugs as well as their identification by microchemical means. Dragendorff in plant chemistry and Behrens in microchemistry were notable European workers of an earlier generation. These men have been followed by Tunmann, Rosenthaler, Molisch and others in the microchemical study of plants and of drugs. Tschirch in his "Handbuch" definitely follows a chemical classification. Driver and Trease have published their "Chemistry of Crude Drugs." However, no American pharmacognocist has thus far presented the chemistry of drugs as a leading part of a pharmacognostical text.

The junior author of this text has acquired, during his studies in Europe, the viewpoint of European pharmacognocists. Therefore this text will reflect his studies on the chemical side of pharmacognosy. This is in accord with the ideas of Dr. Henry Kraemer, who emphasized the need of a knowledge of the chemical constituents of drugs. Note the following quotations from the preface to the second edition of Kraemer's Pharmacognosy: "The study of plant constituents is receiving greater attention and the papers dealing with the microscopical studies are increasing in number. The examination of sublimates obtained upon pyro-analysis of drugs is deserving of greater attention. During the past few years the author has had many students follow this kind of work with a great deal of success. The knowledge of active principles which can be sublimed is increasing and one is almost constrained to say that there are very few drugs which do not yield a characteristic sublimate on igniting the drug. Furthermore, these sublimates can be further tested for identity so that in applying this form of analysis it has a specific value in identifying the drug and may be used as a criterion of its quality. For these reasons this subject has been enlarged upon and new illustrations have been introduced."

In addition to the broader presentation of the chemical ingredients of drugs and their microchemistry, there have been introduced in this new text many new monographs describing official chemical substances obtained from crude drugs; however, these new monographs usually have not been so fully developed as are the monographs of the crude drugs.

Several monographs on crude drugs that have been recently introduced into medicine are included in the text; likewise many new statements bearing on recent investigations of some of the older crude drugs are introduced into the respective monographs.

The illustrations in Kraemer's Pharmacognosy, Third Edition, were remarkably fine and abundant, yet it has been possible to add to these quite a number of illustrations presenting more recent information or a more accurate picture. Particular acknowledgment is due to Raymond S. Adamson, Gerston Bruch and Paul D. Carpenter, for line drawings and photomicrographs. In each case the name of the artist is included in the legend.

The chapter on animal drugs, as published in Kraemer, has been largely rewritten and many new official and unofficial items have been introduced. Especial acknowledgment is due to Dr. Paul Mattis for certain illustrations in the section of this chapter bearing on desiccated glandular products used in medicine.

The use of smaller type for certain portions in the monographs of official drugs and for the entire monographs of unofficial drugs, improves the appearance of the text without impairing its readability, and makes the leading portions of the text stand out more vividly. The portions containing detailed or highly technical descriptions and the text of the unofficial drugs are less prominent because these are of less general interest. Thus we have been able to retain a description or mention of nearly every drug item found in Kraemer's Pharmacognosy, yet also to add many new items without increase in the size of the book.

Particular acknowledgment and thanks are due to Mrs. Minnie Kraemer Harris of Baltimore for permission to use not only parts of the text but also some of the illustrations of Kraemer's Pharmacognosy, Third Edition.

E. N. G.
E. H. W.

CHICAGO, ILL.

CONTENTS

GENERAL CONSIDERATIONS 11
- Definition of Pharmacognosy 11
- History of Pharmacognosy 11
- Study of Drugs 14
- Production of Drugs 17
- Commerce in Drugs 24
- The Pharmacopœia and Formulary 26
- Official and Non-official Drugs 31
- Evaluation of Drugs 32
- Chemistry of Drugs 45
- Analysis of Vegetable and Animal Drugs 51
- Cultivation of Drug Plants 55

THALLOPHYTA 66
- Schizomycetes, or Bacteria 66
  - Vaccines 66
  - Tuberculins 71
  - Toxins, Toxoids and Venins 71
  - Antitoxins and Antivenins 74
  - Antibacterial Serums 76
  - Human Serums and Globulins 77
  - Antibiotic Agents 78
- Algæ 80
  - Bacillariaceæ, or Diatoms 80
  - Phæophyceæ, or Brown Algæ 80
  - Rhodophyceæ, or Red Algæ 82
- Eumycetes, or True Fungi 86
  - Saccharomycetaceæ, or Yeast Family 86
  - Hypocreaceæ, or Flesh-consuming Family 88
- Lichenes, or Lichens 92

BRYOPHYTA 96

PTERIDOPHYTA 97
- Equisetales 97
- Filicales 97
  - Polypodiaceæ, or Polypodium Family 97
- Lycopodiales 100
  - Lycopodiaceæ, or Clubmoss Family 100

SPERMATOPHYTA 102
- Gymnospermæ 102
  - Cycadales 102
  - Ginkgoales 102
  - Coniferales 102
  - Gnetales 116
- Angiospermæ 119
  - Monocotyledoneæ 119
    - Gramineæ, or Grass Family 119
    - Palmæ, or True Palms 143
    - Araceæ, or Arum Family 148
    - Liliaceæ, or Lily Family 150
    - Dioscoreaceæ, or Yam Family 171

SPERMATOPHYTA—(*Continued*)
Angiospermæ—
Monocotyledoneæ—

Iridaceæ, or Iris Family . . . 172
Zingiberaceæ, or Ginger Family . . . 176
Marantaceæ, or Arrowroot Family . . . 184
Orchidaceæ, or Orchid Family . . . 185
Dicotyledoneæ . . . 193
Piperaceæ, or Pepper Family . . . 193
Salicaceæ, or Willow Family . . . 201
Myricaceæ, or Sweet Gale Family . . . 206
Juglandaceæ, or Walnut Family . . . 207
Betulaceæ, or Birch Family . . . 209
Fagaceæ, or Beech Family . . . 209
Ulmaceæ, or Elm Family . . . 216
Moraceæ, or Mulberry Family . . . 219
Urticaceæ, or Nettle Family . . . 222
Santalaceæ, or Sandalwood Family . . . 222
Aristolochiaceæ, or Birthwort Family . . . 223
Polygonaceæ, or Buckwheat Family . . . 227
Chenopodiaceæ, or Goosefoot Family . . . 233
Phytolaccaceæ, or Pokeweed Family . . . 235
Ranunculaceæ, or Crowfoot Family . . . 238
Berberidaceæ, or Barberry Family . . . 252
Menispermaceæ, or Moonseed Family . . . 257
Magnoliaceæ, or Magnolia Family . . . 262
Myristicaceæ, or Nutmeg Family . . . 264
Monimiaceæ, or Monimia Family . . . 269
Lauraceæ, or Laurel Family . . . 269
Papaveraceæ, or Poppy Family . . . 282
Fumariaceæ, or Fumitory Family . . . 294
Cruciferæ, or Mustard Family . . . 294
Droseraceæ, or Sundew Family . . . 303
Saxifragaceæ, or Saxifrage Family . . . 304
Hamamelidaceæ, or Witchhazel Family . . . 304
Rosaceæ, or Rose Family . . . 314
Leguminosæ, or Pulse Family . . . 329
Geraniaceæ, or Geranium Family . . . 361
Linaceæ, or Flax Family . . . 361
Erythroxylaceæ, or Coca Family . . . 364
Zygophyllaceæ, or Caltrop Family . . . 370
Rutaceæ, or Rue Family . . . 371
Simarubaceæ, or Quassia Family . . . 384
Burseraceæ, or Myrrh Family . . . 387
Meliaceæ, or Mahogany Family . . . 389
Polygalaceæ, or Milkwort Family . . . 390
Euphorbiaceæ, or Spurge Family . . . 393
Anacardiaceæ, or Sumac Family . . . 403
Celastraceæ, or Staff-tree Family . . . 407
Aceraceæ, or Maple Family . . . 408
Sapindaceæ, or Soapberry Family . . . 409
Rhamnaceæ, or Buckthorn Family . . . 410
Vitaceæ, or Vine Family . . . 421
Malvaceæ, or Mallow Family . . . 422
Sterculiaceæ, or Cola Family . . . 429
Theaceæ, or Tea Family . . . 435
Guttiferæ, or Gamboge Family . . . 437
Cistaceæ, or Rockrose Family . . . 438
Bixaceæ, or Annatto Family . . . 438

SPERMATOPHYTA—(*Continued*)
Angiospermæ—
Dicotyledoneæ—

Flacourtiaceæ 438
Canellaceæ, or Canella Family 439
Turneraceæ, or Damiana Family 441
Violaceæ, or Violet Family 441
Passifloraceæ, or Passion Flower Family 442
Caricaceæ, or Papaw Family 443
Cactaceæ, or Cactus Family 444
Thymelæaceæ, or Mezereon Family 446
Punicaceæ, or Pomegranate Family 447
Myrtaceæ, or Myrtle Family 449
Araliaceæ, or Ginseng Family 456
Umbelliferæ, or Carrot Family 459
Cornaceæ, or Dogwood Family 476
Ericaceæ, or Heath Family 476
Sapotaceæ, or Gutta-percha Family 482
Styracaceæ, or Styrax Family 483
Oleaceæ, or Olive Family 487
Loganiaceæ, or Nux Vomica Family 490
Gentianaceæ, or Gentian Family 501
Apocynaceæ, or Dogbane Family 505
Asclepiadaceæ, or Milkweed Family 511
Convolvulaceæ, or Morning Glory Family 514
Hydrophyllaceæ, or Waterleaf Family 519
Boraginaceæ, or Borage Family 520
Verbenaceæ, or Vervain Family 521
Labiatæ, or Mint Family 522
Solanaceæ, or Nightshade Family 546
Scrophulariaceæ, or Figwort Family 572
Pedaliaceæ, or Sesame Family 586
Plantaginaceæ, or Plantain Family 587
Rubiaceæ, or Madder Family 590
Caprifoliaceæ, or Honeysuckle Family 610
Valerianaceæ, or Valerian Family 615
Cucurbitaceæ, or Pumpkin Family 616
Campanulaceæ, or Bluebell Family 621
Compositæ, or Composite Family 623

ANIMAL DRUGS 651
- Protozoa 651
  - Foraminifera 651
  - Porifera 651
  - Cœlenterata 651
- Plathelminthes 651
- Nemathelminthes 651
- Annulata 651
- Mollusca 652
- Arthropoda 652
  - Insecta 652
    - Hemiptera 653
      - Coccidæ, or Cochineal Family 653
    - Coleoptera 657
      - Meloidæ, or Blistering Beetle Family 658
    - Hymenoptera 660
      - Apidæ, or Bee Family 660
- Vertebrata 652, 662
  - Pisces 662

ANIMAL DRUGS—(*Continued*)
Vertebrata—
Pisces—

Teleostei 662
Gadidæ, or Codfish Family 662
Reptilia 679
Ophidia 679
Crotalidæ, or Rattlesnake Family 679
Aves 679
Phasianidæ, or Pheasant Family 679
Mammalia 680
Cetacea 680
Physeteridæ, or Sperm Whale Family 680
Carnivora 682
Viverridæ, or Civet Cat Family 682
Rodentia 682
Castoridæ, or Beaver Family 682
Ungulata 682
Artiodactyla 682
Cervidæ, or Deer Family 682
Moschidæ, or Musk Deer Subfamily 683
Perissodactyla 682
Equidæ, or Horse Family 682
Hyracoidea 682
Proboscidea 682
Bovidæ, or Ox Family 683
Suidæ, or Swine Family 691

POWDERED DRUGS 717

KEY FOR IDENTIFICATION OF POWDERS 721

INDEX 732

PHARMACOGNOSY

GENERAL CONSIDERATIONS

THE DEFINITION OF PHARMACOGNOSY

THE term **pharmacognosy** was introduced by Seydler in 1815, and is formed from two Greek words, *pharmakon*, drug, and *gnosis*, knowledge, and literally means the "entire knowledge of drugs." The most comprehensive idea of the scope of pharmacognosy has been given to us by Flückiger, who states that it "is the simultaneous application of various scientific disciplines with the object of acquiring the knowledge of drugs from every point of view."

Pharmacognosy may be defined as the study of drugs having their origin in the plant or animal kingdom. In the broad sense this includes a knowledge of the history, distribution, cultivation, collection, selection, preparation, commerce, identification, evaluation, preservation and use of drugs or economic substances bearing on the health of man or other animals. In a restricted sense, the definition implies a particular knowledge of methods of identification and evaluation of drugs. The study of drugs from the standpoint of their medicinal action or value gradually has become separated from the study of their other characteristics and is known as **pharmacology.**

THE HISTORY OF PHARMACOGNOSY

Tschirch has well said that pharmacognosy dates back further than any of the departments of pharmacy. He rightly states that the old herbalists (rhizotomists) were really the first pharmacognocists, and he considers that Dioscorides, by reason of his writings on medicinal plants, was the first teacher in pharmacognosy.

Pharmacognosy was unusually well expounded by Martius, who, in 1825, published a work entitled "Grundriss der Pharmakognosie des Pflanzenreiches," and may be regarded as a great pioneer in modern pharmacognosy.

Prior to the time of Martius and even later, it was customary for the users of drugs to collect them directly from the living plants and it was necessary for them to properly identify these medicinal plants in the field. The work of the herbalists and systematists of earlier times gradually merges with that of the morphologists of recent years.

Modern pharmacognosy developed from Schleiden, who announced in 1838 that the cell is the fundamental unit in plants and showed that the different tissues are combinations of similar cells. About this time also, herbaceous drugs as such, became quite important in commerce and the necessity of distinguishing and evaluating them developed. Many drugs resemble each other rather closely when viewed macroscopically, but microscopically marked differences in cellular characteristics may be apparent. For instance, Schleiden, who had no knowledge that the several commercial sarsaparillas were obtained from different species of *Smilax,* showed by reason of certain differences in the cells of the hypodermis and endodermis that they must be obtained from different species, which later was proven to be the case.

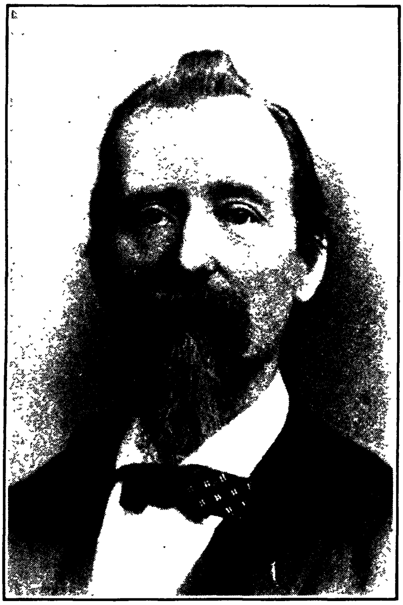


FIG. 1.—John M. Maisch.
1831–1893.

FIG. 2.—Henry Kraemer.
1864–1924.

The histology of plants and animals, hence of drugs, has been highly developed since Schleiden's time and now constitutes one of the basic sciences in applied pharmacognosy.

Among the botanists who have had an important part in the development of **histological** pharmacognosy, which makes the pharmacognosy of today such an exact profession, are O. H. Berg, E. Gilg, H. Molisch, O. E. Oesterle and J. Moeller of Germany; A. Meyer of Austria; A. Tschirch of Switzerland; F. G. Planchon, E. Collin and E. Perrot of France; D. Hanbury, E. M. Holmes and H. G. Greenish of England; J. M. Maisch, H. H. Rusby and H. Kraemer of America.

With the discovery of alkaloids as active principles in drugs by Derosne, Sertüner and Pelletier (1803–1825), the foundations of **chemical** pharmacognosy were laid. Here again during the past hundred years, a great fund of knowledge regarding the chemistry of plants and animals, hence of drugs, has been accumulated. However, it must be said that this information is as yet not nearly so complete as is the histological knowledge. Among the chemists who have played an important part in pharmacognosy are H. E. Merck, H. F. M. Thoms and O. Tunmann of Germany; F. A. Flückiger and A. Tschirch of Switzerland; J. G. M. Dragendorff of Russia; J. O. Schlotterbeck and F. B. Power of America.

The "Pharmacographia" of Flückiger and Hanbury and the "Handbuch" of Tschirch are outstanding works on the history of drugs; the "Pflanzenmikrochemie" of Tunmann laid the foundation for our present microchemistry of drugs; and the "Materia Medica" of Pareira is an early monument in medical pharmacognosy.

Among the noted pharmacognocists of today are G. E. Trease and T. E. Wallis in England; O. Moritz, R. Fischer and G. Karsten in Germany; H. W. Youngken, A. Viehoefer and E. L. Newcomb in America. Among the microchemists are A. Mayrhofer of Germany; L. Rosenthaler of Switzerland; and M. Wagenaar of Holland. A list of well-known books on pharmacognosy is appended.

N. L. Allport: "The Chemistry and Pharmacy of Vegetable Drugs" (1944.)
E. Collin: "Traite de toxocologie vegetale" (1904).
Cooper, Denston and Riley: "A Text Book of Pharmacognosy" (1931).
T. C. Denston: "A Textbook of Pharmacognosy" (1939).
J. E. Driver and G. E. Trease: "The Chemistry of Crude Drugs" (1928).
I. R. Famhy: "Pharmacognosy" (1932).
Robert Fischer: "Praktikum der Pharmakognosie," (1942).
F. A. Flückiger and D. Hanbury: "Pharmacographia" (1879).
Gilg, Brandt and Schürhoff: "Pharmakognosie" (1927).
E. Gilg: "Grundzuge der Botanik für Pharmazeuten" (1921).
O. Giswold and C. H. Rogers: "The Chemistry of Plant Constituents" (1943).
C. B. Gnadinger: "Pyrethrum Flowers" (1936).
H. G. Greenish: "A Text Book of Materia Medica" (1924).
H. G. Greenish and E. Collin: "An Anatomical Atlas of Vegetable Powders" (1904).
H. G. Greenish: "The Microscopical Examination of Foods and Drugs" (3d ed.) (1927).
R. Jaretzky: "Lehrbuch der Pharmakognosie" (1937).
G. Karsten and W. Benecke: "Lehrbuch der Pharmakognosie" (1928).
H. Kraemer: "Scientific and Applied Pharmacognosy" (3d ed.) (1928).
J. M. Maisch: "A Manual of Organic Materia Medica" (1890).
W. Mansfield: "Histology of Medicinal Plants" (1916).
A. Mayrhofer: "Mikrochemie der Arzneimittel und Gifte" (1923–1928).
J. Moeller and C. Griebel: "Mikroskopie der Nahrungs- und Genuszmittel aus dem Pflanzenreiche" (1928).
J. Moeller: "Pharmakognostischer Atlas" (1892).
H. Molisch: "Mikrochemie der Pflanze" (1923).
Otto Moritz: "Einführung in die Allgemeine Pharmakognosie" (1936).
L. E. Sayre: "Organic Materia Medica and Pharmacognosy" (4th ed.) (1917).
A. Schneider: "Microanalysis of Powdered Vegetable Drugs" (1921).
O. Tunmann and L. Rosenthaler: "Pflanzenmikrochemie" (1931).
G. E. Trease: "A Textbook of Pharmacognosy" (1945).
A. Tschirch: "Handbuch der Pharmakognosie" (1932).
A. Tschirch and O. E. Oesterle: "Anatomischer Atlas" (1900).
A. E. Vogl: "Anatomischer Atlas zur Pharmacognosie" (1887).
A. Vrgoc: "Uputa u Farmakognoziju."

O. A. Wall: "Handbook of Pharmacognosy" (1928).
T. E. Wallis: "Analytical Microscopy" (1923).
T. E. Wallis: "Practical Pharmacognosy" (1925).
T. E. Wallis: "Textbook of Pharmacognosy" (1946).
H. C. Washburn and W. H. Blome: "Pharmacognosy and Materia Medica" (1927).
R. Wasicky and co-workers: "Leitfaden fur die pharmakognostichen Untersuchungen im Unterricht und in der Praxis" (1936).
A. L. Winton and K. B. Winton: "The Structure and Composition of Foods" (1932).
H. W. Youngken: "Textbook of Pharmacognosy" (1943).

THE STUDY OF DRUGS

The **natural origin** of a drug is the plant or animal yielding it; if a plant, **botanical origin** or **botanical source** and if an animal, **zoölogical origin** or **zoölogical source.** It is essential therefore that the pharmacognocist have a sound background in **biology.** The scientific **name** and **classification** of the plant or animal yielding the drug, as well as a knowledge of its **morphology** and **histology** are necessary for the **identification** of the drug, hence **zoölogy** and **botany** are essential to the pharmacognocist. A knowledge of the production of the drug, including its **geographical source,** and of **drug plant cultivation,** a feature of increasing importance in pharmacognosy, requires a basic knowledge of **world geography, global economics, horticulture, plant physiology** and **entomology,** as well as **plant ecology and plant genetics. Drug identification** and **evaluation** requires a working knowledge of **plant chemistry, physics** and **crystallography.** Some knowledge of **Latin** is useful in understanding the derivation of scientific names and a reading knowledge of foreign languages, especially **German** and **French** in botany and chemistry, and **Russian** and **Swedish** in horticulture are invaluable in reading original publications.

On the other hand, no amount of reading or scientific training will fully take the place of a real interest in the subject. This can be acquired in the drug store or drug warehouse, in the field or in the college laboratories with their extensive collections.

The Study of Drugs may be pursued from a number of viewpoints. In an artificial system, they may be grouped according to the **parts of plants** which constitute the drug, as roots, rhizomes, leaves, etc. This method has much to commend it in practice, but unfortunately the form of the commercial article is not such that it is always possible to determine whether it should be placed among roots or rhizomes, leaves or herbs, etc. A second system of arranging drugs is according to their important **constituents.** Since the action of drugs is dependent upon these constituents such a chemical classification would seem to be the most rational. As our knowledge of the chemistry of drugs increases there is no doubt that it will become the accepted means of classification. Unfortunately, however, our knowledge of the chemical constituents of drugs is still often meager, and even in those drugs that have been investigated there may be present a number of principles, each of which serves a useful purpose. A third method is to consider the plants yielding drugs according to their **natural relationship.** With our knowledge of morphology, including both organography and the internal structure of a large number of plants, it would seem that this still furnishes the best system for practical pharmacognosy. In a large number of families we find there are certain morphological characters that are more or less distinctive for each: the *Compositæ* contain inulin; the *Labiatæ* have square stems and bilabiate calyxes and corollas, as well as a typical 8-celled glandular hair and usually contain volatile oils; the *Solanaceæ* are abundant in mydriatic alkaloids; the *Umbelliferæ* yield volatile oils, and so on. Furthermore two or more drugs are not infrequently derived from a single plant, and for this reason can be better considered in connection with the products derived from a single plant than if they are placed in widely divergent groups.

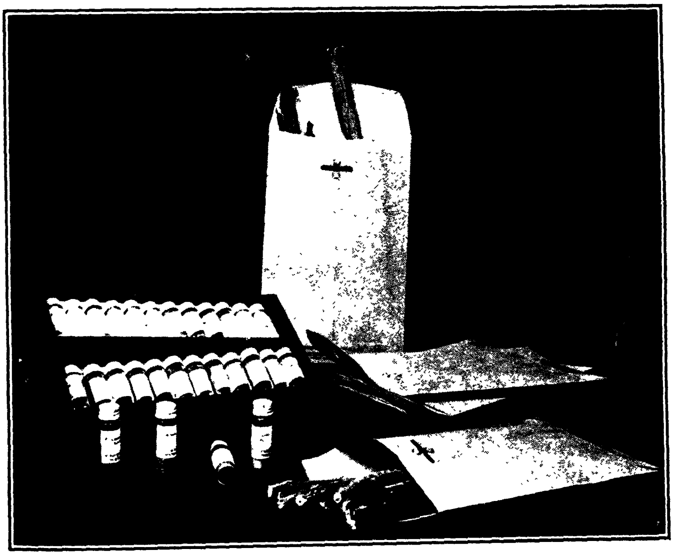


Fig. 3.—Manila envelopes for entire drug specimens, and screw-cap vials in a box with four trays for powdered drug specimens. Used by students at the University of Illinois. (Photo by R. S. Adamson.)

It is important that the student, pharmacist or analyst possess a **collection of authentic drug specimens** both of the entire drug and of the powdered drug. For the determination of the identity and purity of drugs such known samples are invaluable. Specimens may be kept in various kinds of boxes and bottles, or in manila clasp envelopes; the latter utilize a minimum of space, may be filed, and provide abundant space for names and notes on the drug enclosed in them. Another satisfactory way is to keep the drugs in type cases, such as are used by printers, the top being covered with glass which can be removed. This method gives at one time a view of all of the drugs in the case.

The powdered drugs may be conveniently kept in vials in suitable light-proof containers. Where insect attack is likely to occur a few crystals of p-dichlorobenzene added from time to time will keep specimens in good condition.

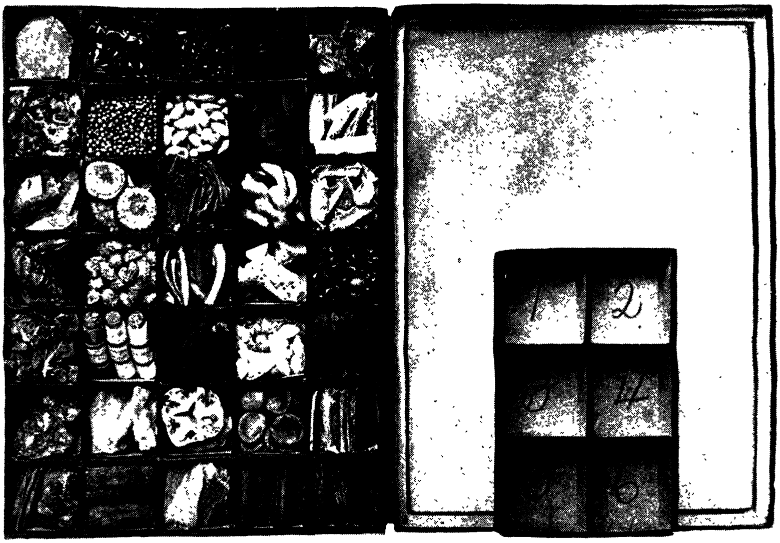


Fig. 4.—Pharmacognosy specimen case constructed of cardboard, covered with black paper muslin and with hinged glass cover, as used by students at the University of Minnesota. The six compartment box is used in presenting specimens to students. (Photo bv Newcomb.)

An organized record of the facts regarding each drug studied should be kept by the student; hence a **note book**, including drawing paper, should be provided. The employment of sketches to record macro- and micromorphological features of drugs cannot be too strongly recommended. Such sketches often illustrate features which would require hundreds of words to describe. Furthermore an **outline form** suitable for systematizing the notes is highly desirable. Such a form commonly used in the laboratory study of drugs, is as follows:

Official Title

1. Latin Title and Synonyms.
2. Definition.
3. Geographical Source (see map of ———).
4. Shape and Size.
5. External Markings and Color.
6. Fracture and Internal Color.
7. Odor and Taste.
8. Structure.
9. Constituents and Standards of Quality.
10. Tests for Identity and Purity and Common Adulterants.
11. Therapeutic Properties and Use.
12. Dose.

THE PRODUCTION OF DRUGS

The Federal Food, Drug and Cosmetic Act defines a drug as follows:

> "The term 'drug' means (1) articles recognized in the official United States Pharmacopœia, official Homeopathic Pharmacopœia of the United States, or official National Formulary, or any supplement to any of them; and (2) articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals, and (3) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (4) articles intended for use as a component of any articles specified in clause (1), (2) or (3); but does not include devices or their components, parts or accessories."

A vegetable or animal drug is then an article of vegetable or animal origin conforming to the above definition. It may be an actual therapeutic agent, it may be a surgical or anesthetic aid or it may be a pharmaceutical necessity, that is a solvent, a vehicle, a sweetening, preserving, flavoring, or coloring agent, or it may be a diagnostic aid. Vegetable or animal drugs which consist of plant or animal parts that have undergone no other processes than collection and drying are sometimes designated as **crude drugs.** They may themselves be used as therapeutic agents or they may, upon further treatment yield products that are used for drug purposes. Any discussion of vegetable or animal drugs must of needs begin with the plant or animal yielding them.

Many plants and animals that produce drugs also produce foods, spices and condiments, narcotics, textiles, lumber, tanning extracts, perfume oils, ornamental flowers and a host of other economic products. The production of such food and economic products often parallels in many ways the production of drugs.

The **geographical source** and **habitat** is the region in which the plant or animal yielding the drug grows. Sometimes this term is applied erroneously to the drugs themselves. Drugs are collected in all parts of the world, though the tropics and subtropics yield more drugs than do the arctic and subarctic regions. The Mediterranean Basin including Asia Minor yields more drugs than any other region of the world. However, India, the East Indies, central Europe, northern South America, Mexico and Central America, North America and other regions yield numerous and valuable drugs.

Neither the scientific name of the plant nor the commercial name of the drug may be relied upon as indicating the true habitat of drug plants. For example, the specific name of *Spigelia marilandica* indicates that the plant is found in great abundance in Maryland, whereas it is only occasionally met with in that state. In other cases plants are common to a much larger territory than the specific name would indicate, as *Prunus virginiana.* Peru balsam, for example, does not come from Peru but is produced in San Salvador, while most of the Spanish licorice now comes from Asia Minor.

Plants growing in their native countries are said to be **indigenous** to those regions, as *Stillingia sylvatica,* of the southern United States; *Aconitum napellus* of the mountainous regions of Europe, etc. Plants are said to be **naturalized** when they grow in a foreign land or in a locality other than their native home. Some of these may have been introduced with the seeds of cultivated plants, some by birds or ocean currents, others by ballast of ships, and so on.

Drugs may be collected from wild plants, or plants may be cultivated for the production of drugs.

Cultivated medicinal plants have been propagated in China, India, Europe and many other lands for centuries past. In Europe, the medicinal plant gardens of the monasteries date back to rather early in the Christian era. With the advent of colonizing, beginning shortly after the discovery of America and continuing almost to the present, many countries made definite attempts to cultivate drug and economic plants in their possessions. Thus vanilla, a native of Mexico and Central America, is now produced at such distances from its original habitat as the Island of Reunion, Tahiti and Mauritius. Cocoa, another native of Mexico, is now produced in large quantities in Nigeria and the African Gold Coast, in Ceylon and in Java. Cinchona, native to the South American Andes, was developed as a crop in Java. By 1900 the South American production was practically nil, due to the destruction of wild trees and the Dutch had a world monopoly on cinchona and its alkaloids. Quite a similar situation exists with coca, another South American plant transported to Java.

In many instances plants have been cultivated in their native habitats, either because of dwindling natural supply, or to improve the quality of the drug. Before World War II the Japanese had established large plantations of camphor trees in Formosa, and held a virtual monopoly in natural camphor. Ceylon cinnamon is entirely produced from cultivated plants, which is also true of cardamom and opium.

Certain areas in the United States are devoted to extensive cultivation of certain drug plants. Areas in southern Michigan and northern Indiana are devoted to the culture of mints, and a large part of our supply of peppermint and spearmint oils come from this region. Carroll County, Maryland, produces a large part of our supply of chenopodium oil. A small area in Washington produces almost our entire supply of hydrastis. Louisiana produces castor oil from cultivated plants. In recent years the State of California has sponsored drug and oil plant cultivation among the farmers in the southern part of the State, and this area produces several million dollars worth of drug and economic products annually, all from cultivated plants.

In addition to the economic reasons there are many other advantages in the cultivation of drugs; definite species and varieties can be controlled; the treatment after collection can be controlled and attack by insects and fungi can be prevented; all resulting in an improved product. In many instances improvements in drugs, especially in their content of active constituents can be produced by breeding and soil studies. Several experiment stations have been established for this type of research as well as for graduate instruction in drug plant cultivation. Among such stations are the Oxford Medicinal Plants Scheme in England, the Beltsville Station of the Bureau of Plant Industry of the United States Department of Agriculture, the Drug Plant Experiment Station of the University of Illinois and the various experimental plots operated in connection with Colleges of Pharmacy at various state universities, particularly Minnesota, Washington and Ohio State.

The cultivation of drug plants is often intricate and involves many problems, the solution of which depends upon specific conditions. A general outline of the principles involved in drug plant cultivation is therefore presented as a separate section on page 55.

Collection of drugs from cultivated plants always insures a true natural source. This may, or may not, be the case when drugs are collected from wild plants. Carelessness or ignorance on the part of the collector may often lead to complete or partial substitution. This is especially true when drugs are difficult to collect or the natural source is very scarce. Many drugs are collected from *wild plants,* sometimes on a fairly extensive scale (tragacanth, senna) where collection is the vocation of the gatherer, and sometimes on a limited scale where collection is an avocation (podophyllum, slippery elm). Since drugs come from all over the world, collection areas are almost universal, and collectors may vary from ignorant natives to highly skilled botanists. In the United States certain areas are particularly noteworthy as collection areas: spigelia, podophyllum, serpentaria, and many other native American drugs are collected in the Blue Ridge Mountain region, and Asheville, North Carolina, is one of the important brokerage centers in the country; green hellebore is extensively collected in New York State and arnica flowers in the Rocky Mountain states of Montana, Wyoming and Colorado.

The proper time of harvesting or collection is during that period when the plant part constituting the drug is highest in its content of active principles and when the material will dry to give the maximum quality and appearance. The following general rules for the collection of various drugs may be given:

1. Roots, rhizomes and barks should be collected in the fall after the vegetative processes have ceased. In rare cases they may be collected in the spring before these processes begin. Roots, especially if they are fleshy, will shrink and remain spongy after drying if collected during the growing season (burdock, marshmallow root, belladonna root).
2. Leaves, or leaves and flowering tops should be collected when photosynthesis is most active, which is usually about the time of flowering and before the maturing of the fruit and seed (belladonna leaf, sage).
3. Flowers should be collected prior to or just about the time of pollination (arnica, marigold).
4. Fruits should be collected near the ripening period, *i. e.,* when full grown but unripe (cubeb, black pepper).
5. Seeds should be collected when fully matured, that is when most of them have ripened, but if possible before the fruits have opened (black mustard).

The influence which the *time of collection* has on the quality of vegetable drugs may best be shown by a few illustrations. It is well known that when the fruits of conium are green they will yield over 3 per cent of coniine, but when they become yellow the alkaloid diminishes rapidly in quantity, and therefore much of the commercial drug will not yield 1 per cent of coniine. The same thing may be said of santonica; when the flower heads are unexpanded they will yield over 3 per cent of santonin, but just as soon as the flowers mature there is a rapid disappearance of the anthelmintic principle. Dealers in insect powder (pyrethrum flowers) know that the flowers gathered when they are closed produce the finest and most powerful insect powder, worth nearly twice as much as that made from the half-closed or open flowers.

The **mode of harvesting** varies with the drug being produced and with the pharmaceutical requirements of the drug. The casual, unskilled native usually collects the drug by hand, and sometimes is careless as regards admixtures and adulterations. When the cost of labor is an important factor, the use of mechanical devices is often successful in economically producing the drug. With some drugs, however, where the skilled selection of plant parts is an important factor, mechanical means cannot replace hand labor (digitalis, tobacco). Most overground parts of plants have been collected by hand in the past. Where speed and reduced cost of production are required they can often be collected by means of mechanical devices such as pickers, mowers, binders and combines. Plant material for distillation (peppermint, spearmint) is cut with a mower and left in the swath to partially dry, then raked together and hauled to the stills. For leaves and herbs the cut plants may be hauled directly to the dryers and after drying, the leaf material may be separated from the stems.

At the appropriate time, crops producing fruits and seeds are best cut with a combination mower and binder; the bundles are placed in shocks and after the desired parts are fully cured, ripened and dried, the fruits and seeds are readily separated by threshing (caraway, flaxseed). Flowers are best collected by the use of a hand cranberry scoop or seed stripper. This is a large "comb" with its teeth far enough apart for the stems to enter but close enough to snap off the flowers. This principle is adopted in the mechanical rotary flower picker, in which the teeth are affixed to a rotating drum (pyrethrum flowers, clover).

Barks are largely removed by hand stripping. When it is not necessary to produce large pieces of bark, it may be separated from the wood by sand blasting, and then separating the bark pulp from the sand by means of flotation in water or by air currents. Where roots or other underground parts of the plant constitute the drug, they may be dug by hand, or such mechanical devices as the plow, the potato digger or the shrubbery-lifter may be utilized. The plow and potato digger are adaptable to shallow rooted plants while the shrubbery-lifter is used for deeply rooted ones. In order to comply with the Pharmacopœia and National Formulary limits on acid-insoluble ash, adhering dirt and sand, etc., all of the soil must be removed from the roots. This is best removed by immediately placing the freshly dug roots in special root washing machines.

Drying the plant material removes sufficient moisture to insure good keeping qualities, prevents molding, the action of enzymes, the action of bacteria and any chemical or other possible changes. It fixes the constituents and facilitates grinding and milling as well as rendering the drug into a more convenient form for commercial handling. Proper and successful drying involves two main principles: temperature control and regulation of air flow. Control of the drying operation is determined by the nature of the material to be dried and the desired appearance of the finished product. The plant material can be either air-dried or subjected to artificial heat. Air drying may be done in the sun or in the shade depending upon the material. Sun drying is adaptable to those items which are not unfavorably affected by the direct action of sunlight. Shade drying is employed when it is desirous to retain the natural color of the drug.

Drying with artificial heat is generally the most acceptable method when skillfully operated. It involves the use of various drying devices which may be either purchased or designed and built. In principle it consists of a closed space spanned by several to many movable screen trays which are arranged to allow free circulation of the heated air; its ventilation is controllable and the source of heat which usually enters at the bottom is also controlled. It should be of such a size that it will conveniently accommodate a little more than the anticipated load. The heat should be such as to maintain an efficient temperature for vaporizing the moisture but not high enough to affect the constituents of the drug and the ventilation such as to efficiently utilize the heat units in the air and then remove the moisture-laden air at the time of saturation. When heat and ventilation are properly controlled the plant material is thoroughly dried and produces a drug of maximum quality both in constituents and appearance. Artificial drying has the distinct advantage over air drying in that it immediately stops enzymatic action. In digitalis for example, the natural moisture content of the leaf is sufficient to cause an enzymatic hydrolysis of the cardiac glycosides as soon as the leaf is harvested. If the leaves are allowed to dry naturally a very rapid hydrolysis of these glycosides occurs.

Leaves and overground plant parts are spread in thin layers on screen trays and are dried at moderate temperatures of about 40° C. to 60° C. providing the active principles are not destroyed by these elevated temperatures. Drugs containing volatile constituents are usually air dried or dried in mechanical dryers at a temperature low enough to prevent loss of their volatile principles. Frequent stirring exposes the material to an exchange of air and hastens drying. The proper point of dryness can usually be determined by the brittleness and snap of the plant parts.

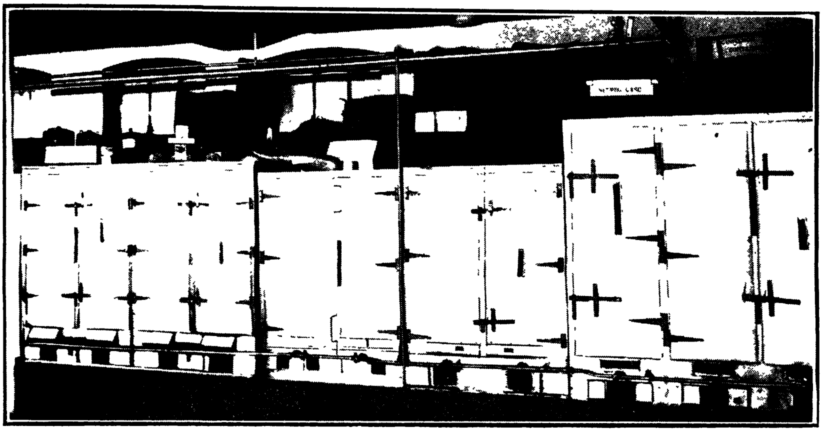


FIG. 5.—Battery of gas-heated drying ovens for the rapid drying of digitalis, belladonna, hyoscyamus and other drugs not injured by moderate temperatures. Drug Drying Laboratory, University of Minnesota.

Roots and rhizomes after being thoroughly washed are carefully and thoroughly dried. Large and fleshy roots such as veratrum viride, belladonna root or burdock root are usually split or sliced to facilitate drying. Where climatic conditions permit, they may be sun dried, but since this process requires from one to two weeks they should be frequently stirred or turned to insure proper ventilation and prevent molding. Time of drying is reduced with artificial heat, but care must be exercised less the exterior layers dry too rapidly and form a crust which retards further drying. The proper point of dryness may again be determined by the nature of the fracture.

Barks are dried either in the sun or shade or by means of artificial heat, depending largely on the constituents. The alkaloids of cinchona bark for example, decompose in the presence of moisture, and drying with artificial heat is necessary to insure a drug of high quality.

Flowers require greater care in drying than other plant parts because their active principles are likely to be less thermostable than those of other drugs. They are usually air dried or at a very low heat in mechanical dryers where proper air circulation can be maintained. Fruits and seeds are generally dry before harvesting and especially before threshing. If not thoroughly dry they may be spread on trays and sun or shade dried before storing in quantity.

With some drugs, as for example vanilla, processes of fermentation or sweating are necessary to bring about changes in the constituents. Such drugs usually require special drying processes.

Garbling is the final step in the preparation of a drug. It consists of the removing of extraneous matter, such as other parts of the plant, dirt and added adulterants. This is done to some extent during collection but should be done after the drug is dried and before it is baled or packaged. Unfortunately it is often not done until the drug has entered commerce when it involves a depreciation in the market value of the lot. It often becomes necessary to garble drugs to enable them to pass legal requirements. In leaf drugs an excess of stems (buchu, senna, uva ursi) must be removed; in rhizomes and tubers, overground stems or stem bases may be excessive (aconite); and in some cases the proportion of roots to rhizomes may be too large. In cypripedium and hydrastis, the roots ("fiber") contain less active constituent, and should be present only in the natural proportion. In some cases particles of iron must be removed with magnets before the drug is ground. Dirt and sand can often be removed by sifting or by means of currents of air. In such cases where the powdered drug may be compressed into tablet form, the damage from sand to dies and punches is very great (veratrum viride). While garbling may in some cases be done by mechanical means it is usually a semi-skilled hand operation.

The **packaging** of drugs is dependent upon their final disposition. If, as is usually the case, this is transportation, storage and ultimate use for manufacturing purposes, it is customary to choose that type of packaging that will provide ample protection to the drug as well as an economy of space. Leaf or herb material is usually baled with power balers into a solid compact mass, which is then sewn into a burlap cover. For overseas shipment such bales weigh from 500 to 800 pounds. Seeds and fruits as well as rhizomes and roots are usually packed in burlap bags and weigh from 100 to 200 pounds. Wooden or corrugated paper boxes and barrels are also common shipping and storage containers. Drugs likely to deteriorate from absorbed moisture (digitalis, ergot) are packed in moisture proof cans. Gums, resins and extracts are shipped in barrels, boxes or casks and vanilla beans in lead or tin lined boxes.

Proper **storage** and **preservation** are important factors in maintaining a high degree of quality of the drug. Warehouses should preferably be of fireproof, steel, concrete or brick construction; they should be unheated and rodent proof. Hard packed bales usually reabsorb little moisture; this is also true of barks and resinous drugs; but leaf, herb and root drugs, not well packed tend to absorb moisture up to 10 per cent, 15 per cent or even 30 per cent, of the weight of the drug. Excessive moisture not only increases the weight of the drug, thus reducing the percentage of active constituents, but also favors enzymatic activity, and facilitates fungal growth. The glycosides in digitalis tend to deteriorate when moisture in the drug reaches 8 per cent or higher. Ergot, gambir, opium, gentian, taraxacum, veratrum viride, aconite, ginger, etc., sometimes occur in a moldy condition. Light adversely affects drugs which are highly colored, rendering them unattractive and possibly producing undesirable changes in constituents. It has been shown that polarized light produces changes more rapidly than ordinary light, and since reflected light is always polarized to some extent, sunlight reflected onto drugs will bring about deterioration. The oxygen of the air increases oxidation of the constituents of drugs, especially when oxidases (oxidizing enzymes) are present. It is therefore very desirable that the warehouse be cool, dark and well ventilated with dry air.

The preservation of drugs against **attacks by insects** must not be overlooked. The insects which infest vegetable drugs belong chiefly to the *Lepidoptera*, *Coleoptera* and *Diptera*. The *Lepidoptera* are the most destructive, and include the cornmeal moth (*Tinea zea*) which during its larval stage is known to attack aconite, capsicum, ergot, lappa, linseed, rhubarb, taraxacum and many other drugs. Among the *Coleoptera* are various members of the *Ptinedæ*, as *Ptinus brunneus*, *Anobium paniceum* and *Lasioderma serricorne*, which attack the spices chiefly, as capsicum, cinnamon and pimenta. Chief among the *Diptera* is *Trypeta arnicivora*, which is sometimes found in the receptacles of arnica flowers. For the destruction of these insects and the prevention of their attacks a number of substances and methods have been employed, the simplest method of all being to expose the drug to a temperature of 65° C. This method is probably the most efficient in not only preventing insect attacks, but all other

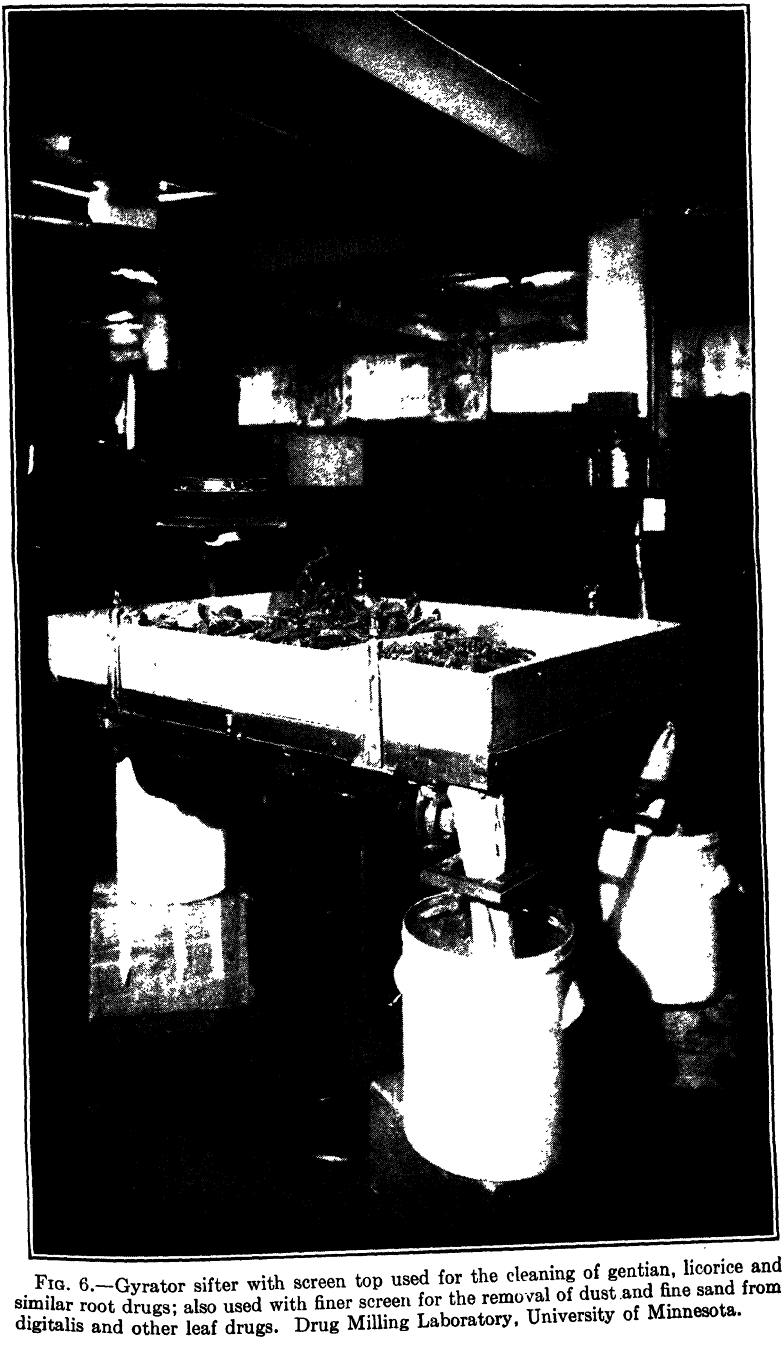


FIG. 6.—Gyrator sifter with screen top used for the cleaning of gentian, licorice and similar root drugs; also used with finer screen for the removal of dust and fine sand from digitalis and other leaf drugs. Drug Milling Laboratory, University of Minnesota.

forms of deterioration. For the fumigation of large lots of crude drugs such as are met with in warehouses and manufacturing plants, the use of methyl bromide has met with considerable success. In a few cases (ginger and nutmeg) insect attack is partially prevented by "liming" which consists of either sprinkling the drug with quicklime or dipping it into a bath of freshly-slaked lime. In these cases, however, an excess of calcium carbonate is considered an adulterant.

Small lots of drugs may readily be stored in air-tight, moisture-proof and light-proof containers. Tinned cans, covered metal bins or amber glass containers are the most satisfactory. Drugs should not be stored in wooden boxes or in drawers and especially not in paper bags. Not only is deterioration hastened, but odors are communicated from one to another, and attacks by insects are facilitated and destruction by mice and rats may occur. Insect attack can be controlled by the addition of a few drops of chloroform or carbon tetrachloride from time to time, provided the container is air tight. In cases such as digitalis and ergot, where a low moisture content must be maintained at all times, the insertion of a suitable cartridge or device containing a non-liquefying, inert, dehydrating substance, may be introduced into the container, which should be air-tight and moisture-proof.

Since high temperatures accelerate all chemical reactions including those involved in deterioration, drugs must always be stored at as low a temperature as possible. An ideal temperature would be just above freezing, but since this is impractical in most cases, the warehouse or other storage place should be as cool as possible. Certain drugs such as the biologicals, must be stored at a temperature not exceeding 5° C.

Animal Drugs are produced from wild or domesticated animals; if from wild animals they must be hunted (whale, musk deer) or fished for (cod and halibut), and so in a sense parallel the collection of vegetable drugs. Many animal drugs however are produced from domesticated animals, and so in a sense parallel the cultivated vegetable drugs. Where drugs consist of insects (cantharides, cochineal) they are collected from wild insects or definite attempts may be made to cultivate them, *i. e.*, to furnish them food and shelter and to maintain optimum conditions for their propagation (honey bee, silkworm). Drugs such as lard, lanolin, milk and milk products, as well as the hormones, the endocrine products and some of the enzymes are obtained from domesticated hogs, sheep or cattle. The slaughter house is their usual source and the large packing establishments all have departments for the recovery and refinement of these therapeutic agents and pharmaceuticals. The processing and purification of the animal drugs vary with the individual drug.

COMMERCE IN DRUGS

The **commercial origin** of a drug refers to its production and its channels of trade. Drugs frequently bear a geographical name indicating the country or region in which they are collected, the country or city from which they are shipped, or to indicate a certain variety. English hyoscyamus leaves are gathered from plants grown in England; Canton rhubarb is the product of plants growing in various parts of China, but shipped by way of Canton; Spanish licorice is a botanical variety of *Glycyrrhiza glabra,* originally produced in Spain but now produced elsewhere, and Virginia snake-root is a species of *Aristolochia* which may or may not come from Virginia. The commercial origin may change in course of time as mentioned in the previous chapter with cinchona, vanilla and coca.

Vegetable drugs are brought into the market in various **commercial forms.** Crude drugs may be nearly entire as seeds, flowers, fruits, leaves, and some roots and rhizomes; or they may be cut, broken or sliced, as in woods, barks, many roots and a few rhizomes. They may be more or less matted together, as in chondrus and the baled leaves; they may be pressed together by hydraulic pressure giving the so-called pressed drugs; or they may be powdered and then molded into forms, as "rhubarb fingers." In some cases the periderm is removed, as in roots (althea), rhizomes (ginger) and barks (slippery elm). Mexican sarsaparilla may come to the market in neat cylindrical rolls in which a mass of the bundled up roots are tightly wrapped by many coils of long roots, or the roots may be in tightly packed bales, or it may be cut into short pieces, or be coarsely ground or finely powdered; each of these forms presents a very different appearance, yet all are the same drug.

Packaging is often characteristic for certain drugs. Socotrine aloe may be packaged in skins, while Curaçao aloe comes in globular gourds of various sizes. Great compressed bales wrapped in burlap, or boxes, barrels and casks, or bags and sacks of various materials are all common forms of packaging. Matting-covered packages of cinnamon from China, seroons of cowhide containing sarsaparilla from South America, square kerosene cans with balsam of Peru from Central America, lead flasks of oil of rose from Bulgaria, shiploads of quassia logs from the West Indies, and many other odd forms of shipment are noted in the drug trade.

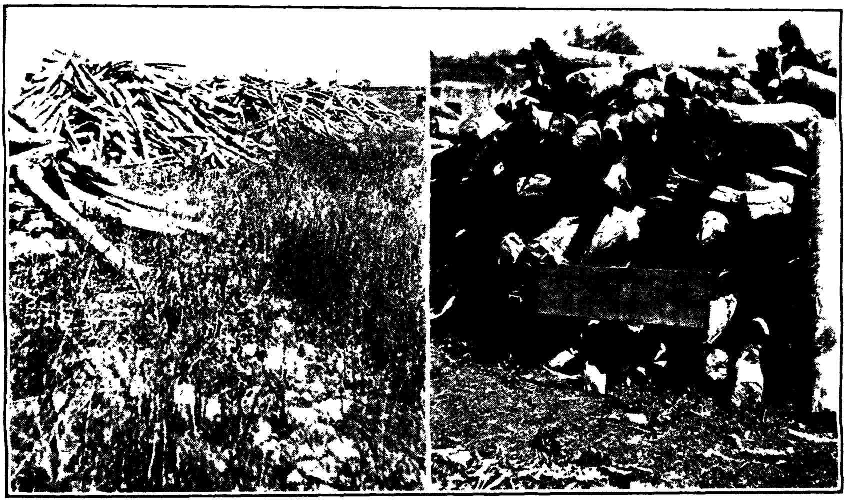


Fig. 7.—Quassia logs at the plant of a pharmaceutical manufacturer near Chicago, after arrival of shipment by boat and train from the West Indies. (Photos by Paul D. Carpenter.)

London and Amsterdam were until recently the great **primary markets** for drugs. Many producers in foreign countries consigned their drugs to brokers in London. When the cargo arrived the brokers obtained samples of the items, and at stated times, placed them on display as "drug shows" the day before the "drug auction." The broker also issued a catalog listing the merchandise on display at his office or warehouse, the date of sale, and other information. This afforded prospective buyers an opportunity to inspect the drugs and be prepared for the auction. Amsterdam was a "free port" and many drugs from the East Indies (coca, cinchona, rubber) were handled through it, without Dutch import and export tariffs.

Many of the drugs arriving at a central port for further distribution were "worked" by "bulking" and "garbling." All of the packages of the same drug in a shipment were opened and emptied onto the floor, then carefully garbled and sometimes graded and then repackaged at variable prices. At this stage some operators were tempted to recondition items of poor quality so that they might pass inspection.

Since World War I there has been a tendency on the part of foreign shippers to sell directly to dealers in Europe and America. Goods are usually purchased prior to shipment. New York City is the principal port of entry into the United States, although Boston, Baltimore, Atlanta, New Orleans and San Francisco also handle some traffic in drugs. All items arriving at these ports are thoroughly inspected by the customs service and by inspectors of the Food and Drug Administration. Before they are permitted to enter they must meet the requirements of U. S. Pharmacopœia, the National Formulary or other standards set down by the Administration.

Since World War II, most of the drug items have been shipped directly to New York from the producing areas. In many of these producing areas, or in small countries, the farmer sells his wares to a local government agency, very commonly the bank of the country. This agency finances and supervises the smaller projects, their collection, grading and packaging and finally arranges for the sale of the drug items, usually by direct contact with the foreign buyer.

Native American drugs are often collected by individuals who in turn sell them to jobbers or directly to manufacturing plants. Large drug brokers such as S. B. Penick & Company have buyers in the collecting areas, and often employ individuals to collect. Some collectors as E. C. Moran, of Stanford, Montana, sell directly to brokers and manufacturers. The small operator, whether he be a collector or producer, must have a knowledge of drug markets, which fluctuate considerably depending upon supply and demand. During the past ten years, belladonna leaf, for example, has sold as low as 17 cents a pound and as high as $3.25 a pound. This, of course, represents an extreme case.

THE PHARMACOPŒIA AND FORMULARY

Drugs of outstanding therapeutic value are standardized in the national pharmacopœias, of which about forty are issued at intervals in the nations of the world. The United States Pharmacopœia has been revised and reprinted decennially since 1820 and until 1940, when the U. S. Pharmacopœial Convention at Washington, D. C. changed the revision period to five years. The Spanish Edition of the U. S. Pharmacopœia is recognized as the national pharmacopœia in Cuba, the Philippines and Puerto Rico and in a number of Spanish-language countries of Central and South America.

The National Formulary was developed by the American Pharmaceutical Association and the first edition was issued in 1888. The second edition was issued in 1896; subsequent editions have been issued concurrently with the Pharmacopœia. The current editions of the Pharmacopœia and the Formulary are authorized in the national and state Pure Food and Drug Laws as the **official** standard for the items they contain. Items that have been official in the Pharmacopœia or the Formulary, but that are not found in the current issues, are designated as **unofficial**; items that have never appeared in either book may be called **non-official.**

The several issues of the Pharmacopœia and the Formulary are designated as follows:

U. S. Pharmacopœia			National Formulary	
Authorized at convention of	Period official	Revision number	Period official	Edition number
1820	1820 to 1831			
1830	1831 to 1842	I		
1840	1842 to 1851	II		
1850	1851 to 1863	III		
1860	1863 to 1873	IV		
1870	1873 to 1882	V		
1880	1882 to 1894	VI	1888 to 1896	I
1890	1894 to 1905	VII	1896 to 1905	II
1900	1905 to 1916	VIII	1905 to 1916	III
1910	1916 to 1926	IX	1916 to 1926	IV
1920	1926 to 1936	X	1926 to 1936	V
1930	1936 to 1942	XI	1936 to 1942	VI
1940	1942 to 1947	XII	1942 to 1947	VII
1940	1947 to	XIII	1947 to	VIII

In this text-book the official period of each item is stated in the monograph on the item.

To give some idea of the extent and scope of these books of official drug standards the following tabulation has been prepared. It indicates also the great movements (rise and fall), as well as the new development in medication during the life of the Pharmacopœia and the Formulary.

It has been difficult to separate these items into this classification. The Pharmacopœial editions from 1820 to 1870, inclusive, contain two sections, namely: Materia Medica (primary and secondary lists) and Preparations. The materia medica consists almost entirely of plant drugs, with a few items derived from animals. Nearly all of the chemical items are in the section on preparations, where full directions are given for their manufacture. Morphine and quinine sulphate appear in the 1830 Pharmacopœia; both are found in the preparations section, with full directions for extracting the alkaloids from opium and cinchona bark respectively.

Hundreds of items first listed as Preparations are now definitely assigned to other groups, such as inorganic and organic chemicals. Pepsin and pancreatin first appeared in N.F. I as preparations, with full directions for preparing them. Cod liver oil, now recognized as a vitamin drug of animal origin, was admitted to the Pharmacopœia of 1850, long before vitamins were known. We have drugs in the Pharmacopœia today that are definitely plant or animal parts, yet are used exclusively for their vitamin or hormone activity; where should they be classed? In the tabulation below, drugs are classed as they are generally assigned today.

A detailed classification of the preparations gives further enlightenment as to the rise and fall of classes of medication, as well as to the great variety of pharmaceutical preparations.

U. S. PHARMACOPŒIA AND NATIONAL FORMULARY DRUGS DERIVED

	FROM PLANTS					FROM ANIMALS					FROM CHEMICALS				
	Crude drugs	Chemicals*	Vitamins	Enzymes	Bacteria, yeasts and molds	Animal parts	Chemicals	Enzymes	Vitamins	Endocrines hormones	Inorganic	Organic	Total materia medica	PREPARATIONS	Grand total
U. S. P. 1820	245	7	..	..	1‡	17	..	..	..	..	101	2	373	267	640
U. S. P. I	264	11	..	..	..	19	..	..	..	..	91	5	390	235	625
U. S. P. II	286	13	..	..	..	20	..	..	..	..	98	9	426	278	704
U. S. P. III	290	18	..	..	..	24	..	..	1§	..	112	6	451	320	771
U. S. P. IV	309	24	..	..	1	20	2	..	1	..	134	9	500	374	874
U. S. P. V	315	26	..	..	1	19	2	..	1	..	160	14	538	437	975
U. S. P. VI	277	43	..	2†	..	19	3	2	1	..	169	18	534	466	
N. F. I	3	2	..	..	..	3	..	4	..	..	5	4	21	408	1429
U. S. P. VII	259	56	..	..	..	22	..	3	1	..	173	27	541	457	
N. F. II	4	2	..	..	..	3	..	1	..	..	6	3	19	444	1461
U. S. P. VIII	227	71	..	2	1	19	4	3	1	2	159	47	537	412	
N. F. III	2	3	..	..	..	4	..	2	..	..	13	3	27	542	1518
U. S. P. IX	168	74	..	3	7	16	4	2	1	3	146	49	473	308	
N. F. IV	139	11	..	..	1	9	1	2	..	..	35	5	203	581	1565
U. S. P. X	130	62	..	1	4	14	4	2	1	6	110	73	404	223	
N. F. V	152	10	..	..	1	8	1	2	..	..	43	9	226	553	1406
U. S. P. XI	107	59	..	1	13	13	5	2	2	9	109	77	397	174	
N. F. VI	123	22	..	..	..	6	1	2	.	6	47	18	225	460	1256
U. S. P. XII	97	69	8	1	19	18	10	1	7	10	106	83	429	231	
N. F. VII	137	28	..	..	..	6	1	3	..	6	63	28	272	464	1396
U. S. P. XIII	76	60	5	..	28	20	4	1	5	17	98	93	407	264	
N. F. VIII	124	32	..	1	4	6	2	3	..	5	81	61	320	403	1394

* Plant chemicals include alkaloids; glycosides; distilled oils and waters; expressed oils and fats; extracted acids, sugars and juices; etc. Such chemicals largely produced synthetically are included in organic chemicals.

† Malt, Malt Extract and Diastase.

‡ Yeast.

§ Cod Liver Oil.

PREPARATIONS	U. S. PHARMACOPŒIA														NATIONAL FORMULARY							
	1820	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	I	II	III	IV	V	VI	VII	VIII
Abstracta, Abstracts	..	..	..	..	..	..	11															
Aceta, Vinegars	3	2	3	4	6	5	4	2	2	1	1	1	..	..	1	3	3	2	1	..	1	1
Acida, Acids	2	3	5	5	8	8	7	8	8	8	5	5	3	1	3	5	3	..	1	1	2	4
Alcohol (Diluted)	1	1	1	1	1	1	1	1	1	1	1	1	1	1								
Ampullæ, Ampuls	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	8	29	18	23
Aquæ, Waters	9	9	9	8	13	14	12	19	13	14	9	10	9	8	3	2	1	1	2	3	3	4
Balsamum	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1					
Boroglycerina	..	..	..	..	..	..	..	..	..	..	..	..	..		1	1	1					
Cæmentum, Dental Cement	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1
Capsulæ, Capsules	..	..	..	..	..	..	..	..	..	..	..	..	12	15	..	..	..	..	..	..	..	9
Cataplasma	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	1	1	1	1	1
Cerata, Cerates	11	11	9	10	10	10	8	6	6	3	3	3	2	..	1	3	4	3	3	2	3	5
Chartæ, Papers	..	..	..	..	..	2	3	2	1	..	..	..	..	..	..	1	2	1	1			
Collodia, Collodions	..	..	..	1	2	3	4	4	4	3	2	2	2	2	4	4	4	5	3	2	2	1
Collyria, Eye Washes	4																					
Confectiones, Confections	6	7	5	5	5	5	2	2	2	..	..	..	..	..	..	..	..	2	2			
Cordiale, Cordial	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1	1				
Curatio, Dressing	..	..	..	..	..	..	..	..	..	..	..	..	..		..	..	..	..	1	1		
Decocta, Decoctions	15	11	12	12	12	12	3	3	1	1	1	1	1	..	1	1	3	1				
Denticoni, Dentalcones	..	..	..	..	..	..	..	..	..	..	..	..	..	1								
Dentifricium, Dentifrice	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1	1
Dentilinimenta, Dentaliniments	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	1	1	
Elixira, Elixirs	..	..	..	..	..	..	1	2	3	2	2	2	2	2	86	91	89	77	66	54	52	39
Emplastra, Plasters	8	9	11	13	16	17	17	15	7	7	6	4	4	3	3	7	13	2	2	1	2	2
Emulsa, Emulsions	..	..	..	..	..	..	..	4	6	4	3	4	4	2	11	12	12	9	6	4	4	4
Essentia, Essence	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1					
Extracta, Extracts	16	16	24	30	34	36	31	34	27	23	13	10	7	5	2	5	13	14	14	14	15	11
Fluidextracta, Fluidextracts	..	..	..	8	25	45	79	87	85	50	27	12	10	7	52	45	53	90	105	72	72	31
Fluidglycerata, Fluidglycerates	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	6	6	1	1	
Gargarisma, Gargle	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1	1	1
Gelata, Jellies	..	..	..	..	..	..	..	..	..	..	..	..	2	3	..	..	..	..	..	1	1	2
Gelatinum, Gelatin	..	..	..	..	..	..	..	..	..	1	1	1	1	1	1	1	1	1				
Glycerita, Glycerites	..	..	..	..	..	5	2	6	6	5	..	..	..	..	..	..	5	5	5	1	1	1
Glycerogelatina, Glycerogelatines	..	..	..	..	..	..	..	..	..	..	4	3	3	3	7	7	6	6	5	6	6	3
Infusa, Infusions	23	20	27	32	31	31	6	5	4	3	2	1	1	..	2	3	4	5	4	3	3	1
Inhalatio, Inhalation	..	..	..	..	..	..	..	..	..	..	..	..	..	1								
Injectiones, Injections	..	..	..	..	..	..	..	..	..	..	..	..	23	42								
Inuncta, Inunctions	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	2			
Lavatio, Wash	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1			
Linimenta, Linaments	9	6	6	6	7	9	10	9	8	8	5	4	4	4	8	11	11	9	10	9	10	10

Liquores, Solutions	11	11	14	19	21	27	26	24	25	25	23	17	16	20	41	45	55	52	37	32	39	41
Lotiones, Lotions	..	..	..	..	..	..	..	..	..	..	..	..	..	2	4	4	4	4	7	6	8	7
Magmæ, Magmas	..	..	..	..	..	..	..	..	..	2	1	2	1	2	..	..	1	1	1	1	2	1
Massæ, Masses	..	..	..	..	..	..	3	3	2	2	2	2	1	..	..	..	1	1	1	..	1	2
Melata et Oxymel, Honeys	3	3	4	3	3	3	2	2	2	1	1	..	..	..	1	1	1	3	3	1	1	
Misturæ, Mixtures	9	5	5	6	8	8	11	4	4	2	2	2	1	1	19	20	20	20	13	4	5	5
Mucilagiones, Mucilages	..	1	2	2	4	4	5	4	4	2	2	2	2	2	3	4	4	2	2	1	1	1
Mullæ, Mulls	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5	5	5			
Nebulæ, Sprays	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	5	5	4	4	4
Odontalgicum, Toothache Drops	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1	1
Olea, Oils (medicated)	1	1	1	2	2	2	2	2	1	..	..	1	1	1	3	3	3	6	6	4	4	3
Oleata, Oleates	..	..	..	..	..	..	2	3	5	1	1	1	1	1	4	4	3	5	2			
Oleoresinæ, Oleoresins	..	..	..	..	5	6	6	6	6	6	2	1	1	1	..	..	..	1	1	3	3	3
Oleosacchara, Oil Sugars	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1	1	1	1	1	
Oleovitaminæ, Oil Vitamins	..	..	..	..	..	..	..	..	..	..	..	..	..	4								
Oxymel (see Melata)																						
Pastæ, Paste	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	8	8	8	8	10	10
Petroxolina, Petroxolins	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	20	18	3	3	1
Pilulæ, Pills	23	13	17	18	19	19	15	15	14	7	5	2	1	1	22	22	24	31	24	13	14	10
Pulveres, Powders	8	3	4	4	7	6	9	9	9	7	6	4	2	1	15	17	19	14	13	7	9	11
Salia, Salts	..	..	..	..	..	..	..	..	..	3	2	2	2	2	7	12	12	11	10	10	10	
Solutiones, Resin Solutions	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2			
Species, Teas	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3	3	3	3	3			
Spiritus, Spirits	7	11	10	10	15	17	20	23	18	15	9	9	8	6	12	9	14	9	11	10	12	14
Stili, Pencils	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3	2	2			
Succi, Juices	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	1	1				
Suppositoriæ, Suppositories	..	..	..	..	..	9	1	2	2	2	2	2	2	1	..	..	1	1	1	1	1	
Syrupi, Syrups	15	14	16	20	23	25	34	32	28	22	18	14	13	12	35	38	45	45	38	25	25	24
Tabellæ, Tablets	..	..	..	..	..	..	..	..	..	..	..	1	47	63	..	..	..	..	8	48	32	51
Tinctoriæ, Tinctures	51	48	56	60	56	57	73	72	64	50	41	31	22	18	33	32	46	50	56	47	54	35
Triturationes, Triturations	..	..	..	..	..	..	2	2	2	2	1	1	1									
Trochisci, Troches	3	3	5	6	9	13	16	15	9	5	2	..	..	1	..	2	9	9	2	1	1	
Unguenta, Ointments	19	18	22	25	23	29	26	22	24	20	18	16	17	20	5	7	11	12	19	21	22	21
Vina, Wines	10	9	10	10	10	9	12	8	8	..	..	..	..	..	12	15	15	15	..	..	..	1
Miscellaneous	..	..	..	..	..	..	..	..	..	..	..	..	..	4	..	..	..	..	..	..	..	2
Totals	267	235	278	320	374	437	466	457	412	308	223	174	231	264	408	444	542	581	553	460	464	403

OFFICIAL AND UNOFFICIAL DRUGS

In U. S. Pharmacopœia XIII and National Formulary VIII (1947), each monograph is headed by the English Title, which is immediately followed by the Latin Title. This is an innovation, for all of the preceding editions of each book had the Latin Title as the first and major title of each monograph. The alphabetical arrangement of the English titles also gave opportunity to group the preparations of the drug adjacent to the drug monograph, and this is considered to be an advantage to physician and pharmacist in the use of the book.

The **Official Title** heads the monograph and is in **English.** This is immediately followed by the **Latin** title. In the case of vegetable drugs, these titles are derived either from the generic or specific name of the plant yielding the drug (gelsemium from *Gelsemium sempervirens* or ipecacuanha from *Cephaëlis ipecacuanha*); from the entire botanical name, if more than one drug is derived from the same genus (viburnum prunifolium and viburnum opulus from *Viburnum prunifolium* and *Viburnum opulus*, respectively); from the generic or specific name combined with the plant part, when two drugs are derived from the same plant (colchicum seed and colchicum corm from *Colchicum autumnale*, or belladonna leaf and belladonna root from *Atropa belladonna*); or from local or native names (opium, sarsaparilla, cascara sagrada).

Synonyms, which are usually vernacular names, are frequently applied to a drug. In the official monographs the use of synonyms is discouraged, for it is considered more proper for trained professional persons such as physicians and pharmacists to use the official titles. Furthermore, the use of synonyms frequently leads to confusion in the collection, the commerce and the dispensing of drugs; for instance the term "snakeroot," which has been applied to at least twelve different drugs, frequently causes uncertainty as to what is wanted.

The **official definition** is given in the leading paragraph of the monograph and includes the botanical or zoölogical source, as well as the name of the part or parts constituting the drug, together with their condition (ripe, unripe, dried, fresh, etc.); in some cases other special features or requirements are given, as the geographical or commercial origin, the time of collection or manner of preparation, etc.

The **official rubric** immediately follows the official definition and includes the standards of strength which the drug must attain. These standards may include the amount of active constituent or the degree of biological activity required of the drug.

The **official description** establishes means to identify the drug and to determine its purity. It sets forth the external appearance of the "whole" drug and usually the appearance of the drug structure when sections are viewed under the microscope. Often a description of the salient features of the powder is also given.

The **official tests** aid especially in the determination of the quality and purity of the drug, rather than the identity, though some tests do serve to identify.

The tests as found in the official drug monographs are not numerous, yet may be classified as follows: (1) morphological, as "Unground Salvia contains no leaves that are broad, dark green or with a cordate base (*absence of other Salvia species*)"; (2) microscopic, as "Powdered Salvia does not contain stellate hairs (*absence of Phlomis species*)"; (3) pharmaceutical, as "Boil 1 part of Chondrus for about ten minutes with 30 parts of water, replacing the water lost by evaporation; the strained liquid forms a thick jelly upon cooling"; (4) chemical, as "Cubeb, powdered or crushed and mixed with sulfuric acid, produces a crimson coloration of the acid."

The **official purity requirements** and **tests** state the limits of permissible foreign matter and often name common adulterants and present means for their detection.

The **official assays** are elaborate tests designed to determine the amount of an active ingredient present in the drug, or sometimes to determine the amount of inert matter present. Drug assays may be (1) proximate, where the alkaloidal content is determined, as with belladonna leaf or areca; (2) extractive, where the amount of extractive obtained with any specific solvent is determined, as the ether-soluble extractive (ginger), the alcohol-soluble extractive (gamboge), or the water-soluble extractive (gambir); (3) physical, such as the determination of the volatile oil content of a drug by distillation (salvia); (4) chemical, such as the assay for hydrogen cyanide in bitter almond; (5) biological, where the effect of the drug upon an animal is compared with the effect of a standard upon the same kind of animal, as the digitalis or ergot assays; (6) colorimetric, where the tinctorial power of a drug is compared with a color standard, as the saffron or cudbear assays; (7) peptic, as the pepsin assay; (8) coagulative, as the rennin assay; (9) diastatic, as the malt assay; and many other kinds.

The **preservation** and **storage** of vegetable drugs is frequently referred to in the official monograph. (For further discussion of this subject see page 22.)

The **official dose** of drugs used internally is usually included in the monograph as a guide to physician and pharmacist, but is not obligatory upon either. Usually the average dose is given, and this for a single oral dose for an adult human. Occasionally an average dose is also given for children, or a daily dose is given (see emetine hydrochloride). Sometimes the dose is specified for animals (see areca), and sometimes it is specified to be given parenterally (see emetine hydrochloride), hypodermically (see epinephrine), or intravenously (see arsphenamine).

THE EVALUATION OF DRUGS

The analytical side of pharmacognosy is embraced in the expression "the evaluation of drugs," for this includes the identification of a drug and the determination of its quality and purity.

The Identification of a Drug

The **identity** of a drug is of first importance, for little consideration can be given to an unknown drug as regards its quality and purity.

The identity of a drug can be established by actual collection of the drug from a plant or animal which has been positively identified from the botanical or zoölogical standpoint. This method is rarely followed except by an investigator of the drug, who must be absolutely sure of the origin of his samples. For this reason "drug gardens" are frequently established in connection with institutions of pharmacognostical research.

A second method of identification is by comparison with a known true sample of the drug in conjunction with a description of the drug. A third method, and the most common among pharmacognosists, is by an acquired knowledge of the several characteristics of the true drug. A classic example of wrong identification is noted in the history of American pharmacognosy. The bark of the highbush cranberry (*Viburnum opulus*), long used in American medicine and official in the Pharmacopœia and then in the National Formulary, became entirely substituted commercially with the bark of the mountain maple (*Acer spicatum*), a similar shrub. This fact was not recognized, and the official description for two decades was that of the substitute and not of the true drug.

The Quality of a Drug

Quality refers to the intrinsic value of the drug, that is, to the amount of medicinal principles or active constituents present in the drug. These principles or constituents belong to a group of non-protoplasmic cell contents and will be found classified into groups in the section on "The Chemistry of Drugs." (See page 45.)

A **high grade of quality** in a drug is of such importance that effort should be made to obtain and maintain this high quality. The most important factors to accomplish this have been covered in the section on "The Production of Drugs," (page 17). They include (1) the collection of the drug from the correct natural source at the proper time and in the proper manner; (2) the preparation of the collected drug by proper cleaning, drying and garbling; and (3) the proper preservation of the clean, dry, pure drug against contamination with dirt, moisture, fungi, filth and insects.

The Purity of a Drug

The **purity** of drugs depends upon the absence of foreign matter. In the collection of a drug and its preparation for the market it is hardly possible to attain a state of absolute purity, and a limited amount of innocuous, extraneous matter adhering to the drug or admixed with it is usually not detrimental. **Foreign organic matter** refers to any part of the plant or plants yielding the drug, except that part or those parts designated as constituting the drug, and to any other plant parts, or vegetable or animal tissues or substances. The permissible percentage of foreign organic matter in a drug is usually specified in its monograph. **Foreign inorganic matter**, such as adhering dirt and sand, may be determined by the acid-insoluble ash method, though some drugs contain acid-insoluble ash that is natural to the drug. In the Pharmacopœia, a maximum of 2 per cent of acid-insoluble ash is permitted, unless otherwise stated in the monograph. **Moisture** is normally present, even in the dried drug, to the extent of from 5 to 10 per cent. An excess of moisture is considered as an adulterant.

Adulteration, in the broad and legal sense, is the debasement of any article.

Adulteration involves:

(*a*) **Sophistication or True Adulteration.**—The addition of a spurious or inferior material to any article with intent to defraud. The addition of wheat flour to powdered ginger, with enough capsicum to restore or enhance the pungency and enough curcuma to maintain the color would be a typical example.

(*b*) **Admixture.**—The addition of one article to another through accident, ignorance or carelessness. If the admixture be done intentionally to defraud, it is sophistication. Buchu containing a few stems or sarsaparilla root with some adhering dirt would class as admixtures. If in any case an admixture exceeds the established standard, it becomes legally an adulteration.

(*c*) **Substitution.**—An entirely different article used or sold in place of the one required or asked for. A complete substitution, even though intentional and fraudulent, is not sophistication, as none of the true article is present. However, all substitution is considered legally as adulteration. Cotton-seed oil sold as olive oil, and American saffron sold as Spanish saffron are examples of substitution.

(*d*) **Deterioration.**—An impairment of the quality or value of an article by the abstraction or destruction of valuable constituents by distillation, extraction, aging, moisture, heat, fungi, insects or other means. Whole cloves from which part of the volatile oil has been removed by distillation ("spent" cloves); ground linseed from which part of the fixed oil has been expressed (linseed cake); lard in which the fats have to some extent decomposed to form fatty acids (rancid lard); powdered squill that has hardened through absorption of moisture; coffee that has largely lost its caffeine through over-roasting; ergot that is moldy; and rhubarb that has become "wormy" are examples of deterioration.

(*e*) **Spoilage.**—A form of deterioration in which the quality or value or usefulness of an article is so impaired or destroyed by the action of fungi as to render the article unfit for human consumption. Many examples of spoilage are found, especially of fresh or canned fruit, vegetables, meats, fish, etc. All drugs which are unfit for human or other animal consumption are legally considered as adulterated.

(*f*) **Inferiority.**—Inferiority, in the broad sense, is any substandard condition from any cause. The more restricted definition as applied to foods, drugs and materials produced by Nature indicates a natural substandard condition. The dried ripe seeds of *Strychnos nux-vomica,* containing less than 1.15 per cent strychnine, would be inferior or substandard drug. If, on the other hand, this drug had contained the required 1.15 per cent of strychnine, but this had been partially abstracted with a solvent, the drug would be considered as adulterated or deteriorated.

Milk, offered for sale at retail, is usually required to contain not less than 3 per cent of butter fat. If milk containing 4 per cent of butter fat has water added to it so as to reduce the butter fat to 3 per cent, it is considered adulterated; but if the same milk has all the butter fat separated from it in the form of cream and then just enough of this cream be restored to the milk so as to give the required 3 per cent of butter fat, it will not be considered as adulterated.

A somewhat similar procedure is being followed with some drugs, notably opium and hydrastis. The standard for hydrastis is not less than 2.5 per cent of ether-soluble alkaloids. Powdered hydrastis containing a higher percentage of alkaloids may be admixed with inferior hydrastis or exhausted hydrastis to bring the amount of alkaloids in the mixture to 2.5 per cent or a little more. Such an admixture is not construed as adulteration, though by some the practice is considered as reprehensible.

Substances used as **adulterants** of drugs are almost innumerable. In addition to those mentioned above, especial mention should be made of pieces of iron or lead used to increase weight as in opium and Burgundy pitch and also inserted into fresh ginseng root; pebbles and sand admixed with asafetida; and large masses of dirt placed in the middle of bundles of sarsaparilla root.

Adulteration of foods, spices and drugs was not uncommon during the early years of the nineteenth century, but seemed gradually to become more prevalent up to the latter years of this century, when it was stated that "of the whole food supply of the country one-seventh is adulterated." One can readily obtain figures in the pharmaceutical journals of 1850 to 1910 showing that something like 50 per cent of the powdered drugs upon the market were adulterated. The trade in spices was even worse, for we read that "the adulteration of spices is a practice so common that we would really be surprised to find goods pass through the grocery trade that are absolutely pure." This condition, of course, could not continue indefinitely, and fortunately a few manufacturers, who valued the reputation of their products even more than the money they could make out of them, lent support to national and state legislation which should fix standards of purity for foods and drugs. This finally ended in the passage of the Federal Food and Drugs Act in 1906, which was followed by coöperative legislation in the various states.

Since this date, with the gradually developed strict enforcement of the laws, gross adulteration of foods, spices and drugs has largely ceased.

In 1938, because of certain shortcomings in the Act of 1906, Congress passed a more comprehensive statute, The Federal Food, Drug and Cosmetic Act, which prohibits the movement in interstate commerce of adulterated and misbranded foods, drugs, devices and cosmetics. The federal law is administered by the Food and Drug Administration, a division of the Federal Security Agency. The Food and Drug Administration maintains its central laboratories at Washington, that having the most to do with drug inspection being the Microanalytical Division. The Administration also maintains branch laboratories and corps of inspectors in the principal cities of the United States. Many of their special analytical methods (not found in the U. S. Pharmacopœia or the National Formulary) are published in Food and Drug Circular No. 1, "The Microanalysis of Food and Drug Products."

The **evaluation of a drug** involves a number of methods which may be classified as follows: (1) organoleptic, (2) microscopic, (3) biological. (4) chemical, (5) physical.

The Organoleptic Evaluation of Drugs

Organoleptic (lit. "impression on the organs") refers to evaluation by means of the organs of sense, and includes the macroscopic appearance of the drug, its odor and taste, occasionally the sound or "snap" of its fracture, and the "feel" of the drug to the touch.

For convenience of description the macroscopic characteristics of a drug may be divided into four headings, viz.: (1) shape and size; (2) color and external markings; (3) fracture and internal color; (4) odor and taste. In some official crude drug monographs the entire description is an organoleptic evaluation and the only means of evaluation that is given. Somewhat different terms are used for describing drugs from different parts of the plant, as follows:

A.—Drugs derived from underground parts of the plant, such as rhizomes, roots, bulbs, corms, tubers, etc., occur either (1) entire, (2) in longitudinal slices, (3) in oblique or transverse slices, (4) cut in small cubical pieces, or (5) broken into pieces.

In **shape** they may be (1) cylindrical, as sarsaparilla; (2) cylindraceous or subcylindrical or nearly cylindrical, as podophyllum; (3) conical, as aconite; (4) fusiform (enlarged in the middle and tapering toward the ends), ovoid (egg-shaped) or pyriform (pear-shaped), as jalap; (5) terete (tapering gradually but nearly cylindrical), as stillingia; or (6) disk-shaped, as calumba.

They may be simple or branched and are frequently curved and twisted. In the case of rhizomes, the direction of growth is often considered. This is usually horizontal, but may be oblique and in a few cases is vertical. The direction may be roughly determined by the attachment of the roots and stem-bases.

Sizes are given as to length and diameter and in the most convenient terms, either millimeters (mm.) or centimeters (cm.). In cases where the shape is conical, the diameter of both wide and narrow parts may be of importance.

The **external color** varies from white (where the drugs have been deprived of the periderm) through yellowish gray, yellowish brown, reddish orange, to even brownish black. It is often more or less gray from clay dust. (See page 38.)

External markings may be classified as follows: (1) furrows—alternating ridges and valleys which are more or less parallel, well-defined, and usually due to the shrinkage of the internal parts caused by drying; (2) wrinkles—fine or delicate furrows; (3) annulations--transverse ring-like markings; (4) fissures —splits extending into the tissues; (5) nodules—rounded outgrowths on the surface; (6) projections, such as roots, stem-bases and buds; (7) scars, such as leaf scars, stem-base scars, root scars, bud scars, bud-scale scars.

The **fracture** has to do with the way the plant part breaks when subjected to sufficient pressure. Often the woody portion fractures in a different manner than the non-woody portion. Terms used in describing fractures are as follows: (1) complete, breaking clean across; (2) incomplete, breaking only part way across; (3) short, a clean smooth break with a quick snap; (4) fibrous, a slow giving break accompanied by resistance and characterized by the projection of fibers from the broken surfaces; (5) splintery, breaking irregularly across into pieces with larger and smaller projecting edges and splinters; (6) brittle, easily broken, usually into many pieces when dropped onto a hard surface; (7) tough, breaking with difficulty; (8) weak, breaking with little effort.

In many cases the nature of the fractured surface is as important as the fracture itself. Terms used to describe the fractured surface are as follows: (1) even, a smooth surface; (2) uneven, an irregular broken surface; (3) granular, having a grain-like appearance; (4) hard, a compact surface; (5) horny, a horn-like surface; (6) mealy, a surface characterized by powdering, usually due to an abundance of starch (starchy); (7) resinous, a smooth glossy surface; (8) conchoidal, a resinous surface characterized by having the surfaces curved in convex and concave fashion; (9) waxy, exhibiting a dull wax-like surface. Other descriptive terms as dull, smooth, rough, etc., are also used in describing the fractured surface.

The color of the fractured surface is known as the **internal color.**

B.—The bark refers to that portion of the woody exogenous stem or root that lies outside of the cambium ring. The majority of official barks have periderm present, yet in some cases, as sassafras and slippery elm, this has been removed. In the entire state, barks occur in three shapes: (1) flat or transversely curved pieces; (2) single quills (rolled from one edge); (3) double quills (rolled from both edges). The most important **measurement** is the thickness of the bark. In the case of quills, both the diameter and the length should also be observed while with flat pieces measurements of the length and breadth may be made.

Barks have two surfaces, an outer and an inner, and both are described. The **external color** of barks on both outer and inner surfaces usually varies from brownish gray to brownish black. The inner surface is usually lighter in color than the outer, and in some cases is almost white.

The **markings** on the outer surface of barks are often characteristic, such as (1) lenticels, (2) lichens with their apothecia, (3) corky ridges, warts or prickles, (4) fissures and (5) adhering mosses. The inner surface may be smooth or marked with fine parallel lines (striations) due to the inner fibers of the phloem. Occasionally crystals are found on the inner surface of barks.

The **fracture** of barks may vary from short and weak to tough and fibrous. The examination of the fractured surface includes **color** and the presence or absence of projecting bast fibers and stone cells. In many cases the nature of the fracture of the cortical region differs from that of the phloem region.

C.—The wood refers to that part of the woody exogenous stem or root that lies inside the cambium ring. That portion of the wood which lies near the cambium ring and still functions in the vegetative process of the plant is known as the sapwood, which is usually white; while the inner layers of wood which have ceased to function in the transportation of sap form the heartwood which is often highly colored. Red saunders is an example of heartwood.

Woods occur in the form of chips, raspings and shavings. Their **external surfaces** are usually striated from fibers or porous from tracheæ. The **external color** varies widely. The **fracture** is usually tough and fibrous while the **internal color** is the same as the external color.

D.—Leaves and leaflets are described with the usual botanical terms. The length and width of the blade is the **size** recorded. The general **shape** of the blade, together with that of the apex, margin and base, are given. The **external markings** include the venation, the texture of the leaf, and the hairs or other characters of the upper and lower surfaces. The **"feel"** of the surface may be described (soft, harsh, smooth). The **color** is included under the description of the surfaces.

Many of the leaves occur in a more or less crumpled condition, and such specimens should be macerated in water and then spread out for study. The **fracture** of leaves unless particularly characteristic is usually of no importance in identification.

E.—Flowers, flower-heads and floral parts such as stigmas, corollas, etc., vary greatly as to **shape.** These shapes are described with the usual botanical terms. In the case of flower-heads or inflorescences, the parts, such as receptacle, involucre, ray- and disk-florets, are described individually. Softening in water often aids the examination of floral parts very materially.

F.—Fruits and seeds vary greatly as to shape. The usual forms are globular, ellipsoidal, ovoid, reniform, conical, etc. Two or three dimensions are to be noted as the case may be. Often only a portion of the fruit is official (bitter orange peel). The usual **markings** of fruits consist of attachment scars and the scars or remains of various floral parts. Many of the fruits, especially the drupes, show a wrinkled pericarp surface. These wrinkles are often characteristically netted or reticulated. Seeds usually show a smooth or minutely pitted testa, hilum and micropyle. Often ridges or furrows locating the hypocotyl or cotyledons are seen. **Color** varies greatly and **fracture** is usually of little importance.

G.—Those items sold as crude drugs which do not possess a definite histological (or cell) structure may be products formed in the metabolic processes of the plant, they may be pathological products, or they may have undergone some special pharmaceutical or physical treatment. The group includes items such as gums, resins, gum-resins, mucilages, oleoresins, inspissated juices, latex, tars, extracts, etc. They may occur in (1) tears, small rounded masses formed naturally as the exudation hardens; (2) angular masses, the broken-up material that has hardened in the container; (3) agglutinated masses, harder portions massed with soft material. Often, however, they occur in a state varying from a liquid to a semiplastic mass. Only in the case of tears is the **size** of importance. In the cases of solids, **fracture** and **fractured surface** are important. **Color** is characteristic but characteristic **external markings** are usually absent.

H.—Items such as volatile and fixed oils, glycosides, alkaloids, etc., are usually considered from the chemical standpoint for they have no morphological characters. They will be considered in the drug monographs under the heading of Active Constituents.

I.—A miscellaneous group comprising such items as starches (amylum), excrescences (galls), trichomes (lupulin), sclerotia (ergot), diatom frustules (purified siliceous earth), etc., are of relatively rare occurrence, but the usual characteristics of **size, shape, color, markings,** etc., are determined either macroscopically or microscopically.

The **odor** of a drug may be either distinct or indistinct, depending upon the amount of volatile constituents the drug possesses. General terms used in describing odor are aromatic, balsamic, spicy, alliaceous, camphoraceous, terebinthinate, etc. These terms are comparative with other substances in Nature. When no such correlation can be made and the odor is distinct, it is said to be characteristic.

Taste may be defined as a particular sensation excited by certain substances when these are brought into contact with special organs situated in portions of the epithelial layer of the mouth. It is that sense by which we perceive the characteristic or distinctive savor of soluble substances when these are placed in the mouth and moistened with saliva. The taste of a substance is the quality or savor of the substance perceived in this way. Substances may be classified according to taste into the four following groups:

1. Those possessing a true taste, that is, exciting the sensation referred to above. Such tastes are (*a*) acid or sour, (*b*) saline or salty, (*c*) saccharine or sweet, (*d*) alkaline, (*e*) bitter.

2. Those possessing no taste, and hence are tasteless or insipid. This group includes all substances insoluble in the saliva.

3. Those possessing a characteristic odor which gives name to the so-called "taste." With this a true taste may or may not be associated. Such tastes may be grouped broadly into those which are agreeable, including (*a*) aromatic, (*b*) balsamic, (*c*) spicy; and disagreeable, including (*i*) alliaceous, (*ii*) camphoraceous, (*iii*) terebinthinate.

4. Those imparting distinctive sensations to the tongue, exclusive of taste or touch. These sensations may or may not be associated with true taste. Such substances may be classified as: (*a*) mucilaginous, those producing a soft slimy feeling; (*b*) oily, those producing a bland smooth feeling; (*c*) astringent, those producing a contraction of the tissues of the mouth, causing a puckering feeling; (*d*) pungent, those producing a warm biting sensation; (*e*) acrid, those producing an unpleasant, irritating, tingling sensation; (*f*) nauseous, those tending to excite vomiting.

A drug frequently gives more than one taste, the sensations usually being observed in consecutive order. The first taste noted is produced by the most soluble constituent.

The **color** of drugs whether whole or powdered or in microscopic section is determined by the Inter-Society Color Council-National Bureau of Standards method. The color names indicated in the official monographs are official standards of equal importance to the other organoleptic specifications.

Color names are standardized and each consists of a hue name, with or without one or two modifiers to describe the value (lightness) and chroma (strength) of the hue. In reading colors standard Munsell charts are used and the Munsell notation determined. This is then translated into color nomenclature by the use of ISCC-NBS charts. The National Formulary includes a complete description of the application of the method.

The Microscopic Evaluation of Drugs

The **microscope** has been employed in the examination of drugs since 1847, when Schleiden used it in the examination of the sarsaparillas. In 1853 Schacht showed its value in the examination of textile fibers. The earliest reference in English to the use of the microscope as a means of detecting the admixture or adulteration of drugs is the statement of Professor Pereira in his introductory lecture before the Pharmaceutical Society of Great Britain in 1851, when he said: "You are doubtless conversant with the recent very extensive employment of the microscope for disclosing the adulteration of food. No less useful —no less powerful is it in disclosing the contamination of drugs; and I cannot too strenuously recommend you to employ it."

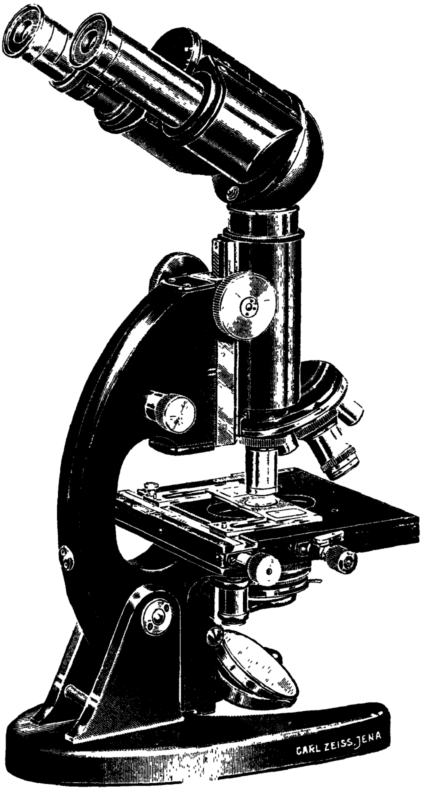


FIG. 8.—Modern compound microscope for research and routine work. Most microscopic examinations may be satisfactorily made without the elaborate equipment shown above, which fits the microscope for photo-micrographic work and any variety of research examinations. A swing-out adjustable condenser, mechanical stage, binocular tube and other accessories are all features of this instrument.

The investigations of Pereira, Hassal and others showed even at that time not only that the microscope had unlimited valuable practical applications, but that it was the only means which had been discovered to detect the admixture or adulteration of non-crystalline organic substances. An article published in the *American Journal of Pharmacy* in 1853 (pages 45–48) on the use of the microscope in the examination of drugs shows that, in spite of the fact that it had only recently come into general use, its value was very early appreciated.

The microscope, however, is not only essential to the study of **adulterants** in powdered plant and animal drugs, but is of indispensable value in the **identification** of the pure powdered drug. Those sections of the official monograph headed **histology** and **powder** deal almost exclusively with the microscopic appearance of the drug in sectional view and powdered form.

Plant parts are made up of tissues, each of which performs a definite function essential to the life of the plant. The histology refers to the character and arrangement of these tissues as they are present in the drug. Some drugs have no cellular structure, as acacia or rosin; some are composed of microscopic units, such as spores (lycopodium) or hairs (lupulin or kamala); with others a knowledge of structure would not be helpful, for they are easily identified macroscopically (chimaphila), or consist of several plant parts (sambucus, adonis); but many drugs possess a characteristic structure helpful in identification of the drug. Histological studies are made from very thin transverse or longitudinal (radial and tangential) slices properly mounted in suitable stains, reagents, or mounting media.

Powdered drugs possess very few macroscopic features of identification outside of color, odor and taste, hence the microscopic characteristics are very important. In the powdered drug (which should be reduced to not less than a No. 40 powder) the cells are mostly broken, except those with lignified walls, but the cell contents (starch, calcium oxalate crystals, aleurone, etc.) are scattered in the powder and become very evident in the mounted specimen.

To prepare a **mount,** transfer a suitable quantity of the powder to 2 or 3 drops of reagent or mounting medium on the clean slide and mix it well with the liquid. Place the cover-slip and by light pressure move the cover-slip in rotary motion to insure an even distribution of the powder under it. A properly prepared mount will just fill the space between slide and cover-slip and will be slightly opaque.

The proper **reagent** or **mounting medium** to be used depends on the characteristic tissue element or cell content to be studied; starch is best examined in water mount; lignified tissue such as bast fibers, stone cells, tracheæ, etc. in a phloroglucin mount; calcium oxalate, leaf epidermal tissue, trichomes, etc., in a chloral mount. Special test reagents as iodine, zinc chloriodide, ferric chloride, etc., are also used where occasion demands.

Not only is the microscope useful in the study of the histological elements of drugs and in the detection of adulterants, from the histological standpoint, but it can be used for the **quantitative microanalysis** of admixed or adulterated powders. This is done by counting a specific histological feature in a measured quantity of the unknown powder and comparing the count with that obtained of the same feature in a known standard sample, which sample may be of the designated powder itself, or of the adulterant, or of any one of the mixture of powders. Similar methods are used for the counting of mold filaments, mold spores, bacteria, etc.

There is a growing interest in **microchemistry,** that is the study of plant constituents by the application of chemical reagents to microscopic sections of the drug or to a small quantity (a few milligrams) of the powdered drug. Microchemistry affords a means by which the constituents of many drugs may be isolated and identified.

The more common microchemical processes are as follows:

I. Isolation of Constituents.

A.—**Isolation With a Solvent.**—1. Five to 10 mg. of the powdered drug material are placed in a small ($\frac{1}{2}$ by 3 inches) test-tube and from 0.5 to 1.0 cc. of a suitable solvent added. The test-tube may be corked or covered with the thumb, and shaken; or heat may be applied to facilitate extraction. Two to 3 drops of the extract are filtered onto a slide and the solvent allowed to evaporate. The residue is now ready for identification.

2. Extraction may also be made directly on a slide. A few milligrams of the powder are placed in a little pile on the slide, a cover-glass being laid in such a manner that the pile is near one edge and the cover-glass lies at a slant. The solvent is placed at the edge of the cover-glass, flowing thereunder and extracting the powder. If the constituent is crystalline, crystals often appear at the opposite edge, and if reasonable care is exercised most of the mount will be free from particles of the powder.

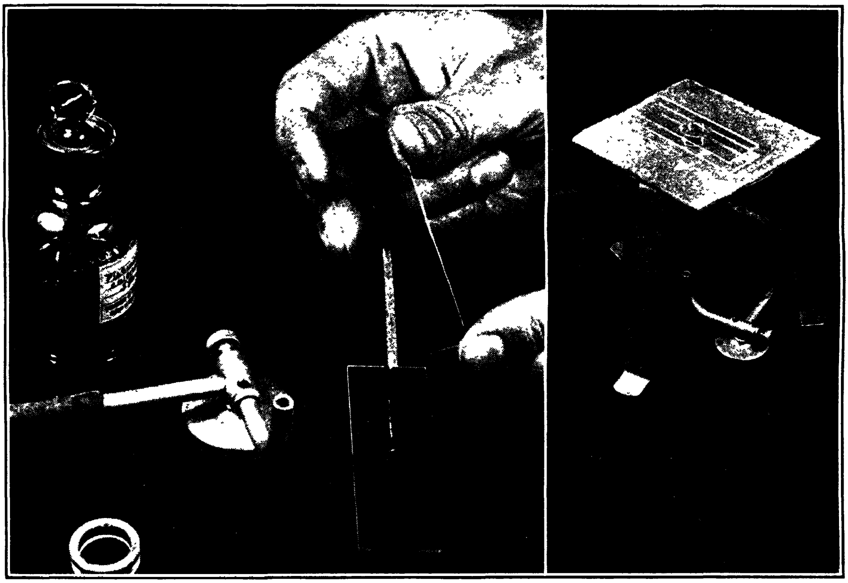


FIG. 9 FIG. 10

FIG. 9.—Microfiltration.
FIG. 10.—Microsublimation. (Photos by E. H. Wirth.)

3. The powdered drug material may be extracted by stirring with a few drops of solvent on a slide, the extract being filtered to a second slide by **microfiltration,** which is accomplished by cutting a strip of filter paper about 5 cm. long into a V-shape, the broad end being 2 to 3 mm. wide. The paper is moistened with the solvent and placed upon the extraction slide so that the broad end is in contact with the solvent and drug. The extraction slide is now held in tilted position in such a manner that the pointed end of the filter paper hanging over the edge will drip the extract upon the receiver slide.

B.—**Isolation by Microsublimation.**—If the constituent is sublimable without decomposition (and very many drug constituents are), microsublimation offers a very convenient method for its isolation, often in a purified state.

Microsublimation may be carried out in several ways:

1. A few milligrams of the powdered drug material are placed in a shallow watch-glass, a slide being placed over the powder in such a way as to rest upon

the edges of the watch-glass, leaving a distance of 1 to 2 mm. between the upper surface of the powder and the lower surface of the slide. Heat is carefully applied and sublimable constituents are collected upon the under surface of the slide.

2. The powdered drug material may be placed on a slide and the receiver slide placed obliquely above it in such a manner that one end of the receiver slide rests upon the sublimation slide, the other being supported by a small piece of wood, the distance between powder and receiver slide being about 1 to 2 mm. Both methods allow some escape of the sublimable material.

3. A third and better method is to place the powdered drug material on a slide, covering it with a glass ring about 1 cm. in diameter and 2 to 4 mm. high, over which the receiver slide is placed. The edges of the ring are ground, thus forming a rather tightly closed chamber within which microsublimation may proceed. If the whole is placed upon an asbestos plate (about 4 by 4 inches) having a 1 cm. hole in the center, heat may be applied without unduly raising the temperature of the receiver slide, sublimation being then more efficient.

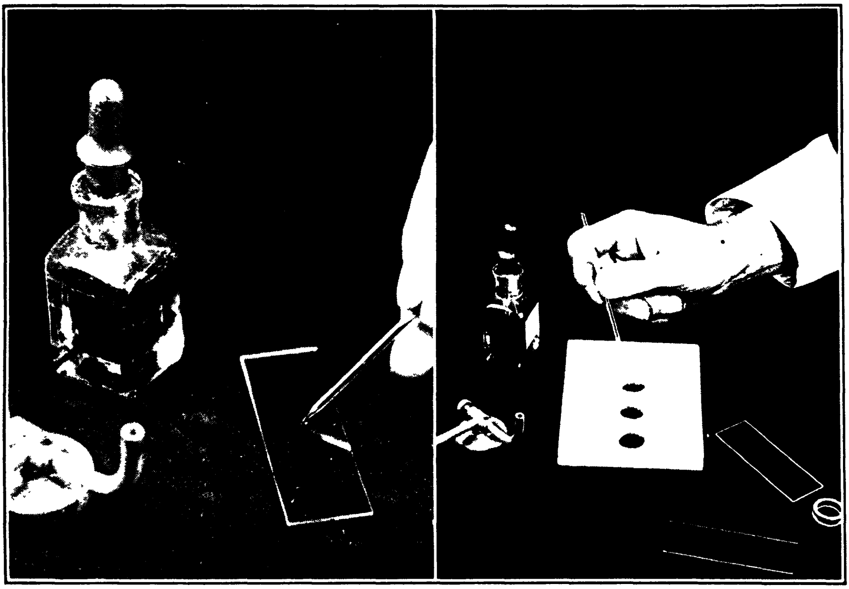


FIG. 11 FIG. 12

FIG. 11.—Testing with reagents on slide.
FIG. 12.—Testing with reagents on spot plate. (Photos by E. H. Wirth.)

II. Identification of Constituents.

After the constituents have been isolated, and further purified, if necessary, by either resublimation or recrystallization, they may be identified by:

1. The crystal system, the forms present and the habit of the crystals themselves.
2. The melting-point of the crystals, obtained by using the thermal stage.
3. Optical crystallographic characteristics, such as whether the crystal is isotropic or anisotropic, uniaxial or biaxial, its type of extinction, optic sign, sign of elongation, its refractive indices, etc.
4. Reagents, which may produce new crystalline reaction products or color reactions.

Many reagents give characteristic color reactions with certain compounds. Such color reactions are of value not only in the identification of reaction products but may also be applied to the original sublimates or to the extracted material, and in many cases to the original drug material. Color reactions are best carried out on a white porcelain spot plate, but may be carried out in an evaporating dish or even on a slide, provided the slide is held against a white background.

Finally, the use of the petrographic microscope with its attachments is of great value in the determination of the optic constants of crystalline substances, thousands of which are now to be found in reference tables. This involves a knowledge of both crystallography and the optics of crystals, but offers an extremely rapid method for the identification of very small amounts of chemical compounds.

The Biological Evaluation of Drugs

Within recent decades the pharmacological activity of certain drugs has been applied to their evaluation and standardization. A rather distinct group of specialists known as bioassayists has developed, and their work constitutes an important phase of pharmacognosy.

Time and space will not permit of a detailed description of the various types of biotests and bioassays but a brief mention can be made of the organisms used and the methods employed, as follows:

1. Bacteria, such as *Eberthella typhi* and *Staphylococcus aureus*, are used to determine the phenol coefficient or antiseptic value of certain drugs, such as thymol in Liquor Antisepticus, N. F. A definite quantity of a recent bouillon culture of the organism is brought into contact with the specified quantity of the antiseptic agent for a definite length of time. If the living bacteria in the quantity of culture taken are all killed during the test, the antiseptic agent meets the required standard.
2. Microbiological methods are in common use in the assay of many of the vitamins. Yeast, *Saccharomyces cerevisiæ* is used in the assay of thiamine, while *Lactobacillus casei* is used in the assay of riboflavin, biotin and pantothenic acid and *Lactobacillus arabinosus* in the assay of nicotinic acid. A mold, *Neurospora sitophila* is used in the pyridoxine assay.
3. Living, microscopic, more or less transparent animal organisms, such as *Daphnia* species, suspended in a microscopic mount, can be observed under the microscope while being treated with certain drugs, such as cascara sagrada or digitalis. A dilute extract of the drug is added to the mounting fluid, it is absorbed to some extent by the minute animals and the pharmacological effect is noted. With cascara sagrada a marked cathartic action with rather rapid evacuation of the alimentary tube is noted; with digitalis the effect on the heart is very vividly portrayed. By quantitative methods, the quality of the drug can be gauged.
4. The use of **goldfish** for the standardization of digitalis and similar "heart tonic" drugs has been proposed and tried out. The fish are placed in known high dilutions of the drug kept at a standard temperature and are transferred from one dilution to another of slightly greater concentration until a dilution is reached that kills the fish within a certain length of time.
5. The use of **frogs** for the standardization of digitalis and other members of this group of drugs, was the official method. The properly prepared dilution of the extract of the drug is compared with a similar preparation of standard digitalis. These dilutions in known quantity are injected into the ventral lymph sacs of frogs and a comparison of the exposed hearts is made. The end-point is the stoppage of the heart in systole.
6. Ergot is sometimes standardized by noting the change in color from red to blue of the combs of **White Leghorn cocks** after they have been injected with an extract of the drug in various dilutions. A comparison is made with cocks injected with standard solution of ergotoxine ethanesulfonate.

7. Vitamins are standardized against **rats** or **mice** by noting the results on healthy standard animals that are deprived in their diet of the specific vitamin.

8. Toxins and antitoxins (diphtheria and tetanus) are standardized on **guinea-pigs** of definite weight. The lethal dose of toxin is known as the "toxic unit." An antitoxic unit is that amount of the antitoxin that will preserve the life of the guinea-pig against 100 toxic units of the toxin injected into the animal at the same time.

Posterior pituitary glandular material is standardized by noting the degree of contraction of the isolated guinea-pig uterus in an oxygenated saline bath when exposed to variable dilutions of an extract of the drug. The test is a comparison with standard drug.

Aconite is also tested on guinea-pigs. The suitably diluted tincture is injected subcutaneously and the time of death is noted. A comparison is made with a suitably diluted solution of standard aconitine.

9. **Cats** may be used for the standardization of digitalis and similar drugs of this pharmacological group. A definite quantity of a known dilution of the drug is transfused into the blood stream of the cat and the lethal effects are noted and compared with a similar dilution of the standard digitalis.

The **Cat's-eye Test** is of interest in evaluating mydriatic drugs, such as atropine. A highly dilute aqueous solution is dropped into the cat's eye and the degree of mydriasis is noted.

10. **Dogs** have been used to standardize cannabis by noting the degree of incoördination in the dog after it has received by mouth a known quantity of an extract of the drug.

11. **Humans** have long offered a valuable means of noting the activity of drugs. Only recently, however, have drugs been officially standardized on humans. These are drugs such as liver, stomach and other preparations which are used for the treatment of pernicious anemia.

Chemical Evaluation of Drugs

The evaluation of crude drugs by chemical means is followed only to a slight extent. The active constituents of crude drugs, especially when separated and highly purified, are, however, evaluated **largely** by **chemical means.**

Chemical tests employed to determine the identity or purity of cellular drugs are relatively few and have already been referred to. Among such tests mention should be made of the determination of acid-insoluble ash and of crude fiber. **Chemical assays** of crude drugs also are scarce, perhaps the assay of black mustard being the only one that is strictly chemical among all of those applied to official crude drugs. The usual alkaloidal assays are extractive processes (pharmaceutical), with subsequent purification of the alkaloid. If the alkaloid be determined gravimetrically, the whole assay is pharmaceutical. If it be determined *by titration, the assay does have a chemical phase. All of the other* types of assays (see page 32) are strictly pharmaceutical processes except the bioassays which are pharmacological in nature.

Microchemical tests (see page 40) on crude drugs may have a chemical phase, though often not. As they require the use of the microscope for their reading, it seems desirable to include them under the microscopic evaluation of drugs.

Those drugs of plant or animal origin that are non-cellular in nature or that represent active principles from the plant (see page 33) lend themselves more readily to chemical study. The isolation, identification, purification and characteristics as determined by tests and assays, are to some extent of a pharmaceutical nature, yet to a large extent they are chemical. The determination of the saponification value, the iodine value and the acid value of fixed oils might be mentioned as illustrations. Styrax and atropine represent typical drugs of plant origin for which extensive chemical tests have been devised.

The Physical Evaluation of Drugs

So far as crude drugs are concerned, the application of typical physical constants is very rare. Occasionally the **specific gravity** is a matter of interest, as with nutgalls, where the galls that will not sink in water are considered to be of inferior quality, and as with jalap, where its specific gravity should be higher than water. The **elasticity** of certain fibers, such as cotton, is a physical constant of importance. The reaction of certain drugs either in powdered form or on their smooth sectional surfaces, with filtered **ultra-violet light** is of importance in several cases, notably rhubarb, where the genuine Chinese Shensi rhubarb can easily be distinguished from rhapontic rhubarb by the difference in luminosity in this light. The light is also used for determining fluorescence and a play of colors in connection with certain extracts, such as chlorophyll and the extracts of certain drugs such as catechu, senna leaves, etc. Many alkaloids show distinctive colors under this light, such as aconitine (light blue), berberine (yellow), emetine (orange). An alkaloid such as quinine which shows a fluorescence in acid solution even in daylight, shows such fluorescence much stronger under the quartz lamp. Many other drugs show a marked intensity of color or characteristic color under this light.

The application of physical constants, however, is extensive in connection with certain active principles from the drugs such as alkaloids, volatile oils, fixed oils, etc. The physical constants that are generally used in connection with such drugs are as follows: (*a*) **solubilities** (usually expressed in the following form: 1 Gm. is soluble in — cc. of water, — cc. of alcohol, etc.), (*b*) **specific gravity** (particularly of the fats and volatile oils), (*c*) **optical rotation** (of certain alkaloids in solution and of the volatile oils), (*d*) **refractive index** (particularly of the volatile oils and the fixed oils), (*e*) **congealing point** (particularly of the volatile oils and fixed oils), (*f*) **melting-point** (particularly of the solid fixed oils and of some alkaloids), (*g*) **water content** (as determined by drying to constant weight in an oven).

THE CHEMISTRY OF DRUGS

The living plant is nature's laboratory. Therein are synthesized not only chemical compounds that are utilized as food by man and animals (carbohydrates, proteins, fats), but also a multitude of compounds that exert a physiologic effect. It is because of these chemical compounds that drugs are used as, or are the source of therapeutic agents. It is obvious therefore that any study of pharmacognosy must embrace a thorough consideration of these chemical entities. The usual term for them is "constituents"; but since the plant, as is true of any organism, is composed of many chemical compounds, it is common practice to single out those compounds that are responsible for the therapeutic effect and call them "**active** constituents."

For purposes of classification it is logical to arrange these compounds into groups according to their constitution. It is, however, not the purpose of this introductory section to discuss each of these groups in detail. Such discussions will be found throughout the text in appropriate locations where important drugs belonging to the particular group are discussed.

1. **Carbohydrates.**—Carbohydrates are aldehyde or ketone alcohols containing carbon, hydrogen and oxygen in which the hydrogen and oxygen are in the same ratio as in water. Since carbohydrates are the first products formed in photosynthesis, they are a convenient starting point for any discussion of constituents of vegetable drugs. Moreover they are the products from which, by subsequent organic reactions the plant synthesizes a great number of other constituents. The photosynthetic reaction is expressed as follows:

$$6CO_2 + 6H_2O\ (+\ 677.2\ \text{cal.}) \rightarrow C_6H_{12}O_6 + 6O_2$$

When plants or animals utilize carbohydrates as food the 677.2 calories are released and the reaction of *respiration* is simply the reversal of the above. These (photosynthesis and respiration) are the most important chemical reactions with relation to the maintenance of life upon the earth.

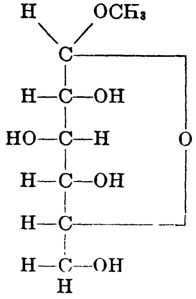
Carbohydrates are classified according to their constitution. Those having six carbon atoms ($C_6H_{12}O_6$) are called *hexoses* or *monosaccharides;* those having twelve carbon atoms ($C_{12}H_{22}O_{11}$) *disaccharides;* those having eighteen carbon atoms ($C_{18}H_{32}O_{16}$) *trisaccharides,* etc. Such simple carbohydrates, because of their solubility and sweet taste are commonly referred to as sugars (page 128). The more complex, high molecular weight polysaccharides are represented by starch (page 119), inulin (page 624) and the celluloses (page 426). These polysaccharides can usually be hydrolyzed to a component hexose and are therefore called hexosans: starch which yields dextrose is known as a *dextrosan,* while inulin yielding levulose is known as a *levulosan.* Sugars and starch are important products in the economy of mankind. They are extensively used as foods and pharmaceuticals.

The plant also builds its structural skeleton from carbohydrate material. The name *cellulose* is given to a group of closely allied cell wall substances, having in common a portion of the molecule that is an anhydride of glucose. Other substances occur with cellulose as for example, the hemicelluloses. These are also high-molecular weight celluloses but differ from cellulose in being considerably more soluble and more easily hydrolyzed. Closely related to the hemicelluloses are the *gums* and *mucilages* (page 333) which constitute an important group of drugs both from the pharmaceutical as well as the therapeutic viewpoint. Also associated with cellulose are the *pectins* (page 376) which have some pharmaceutical application.

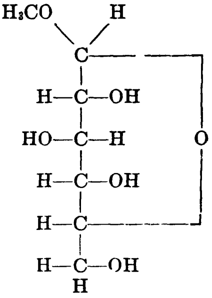
No summary of the carbohydrates is complete without mention of the pentoses and pentosans. The name pentose is applied to a group of sugars having the general formula $C_5H_{10}O_5$ (arabinose, xylose, ribose) and are usually products resulting from the hydrolysis of the pentosans, of which xylan, occurring in the wood of deciduous trees, is an example. Pentoses also result from the hydrolysis of gums and mucilages.

2. **Glycosides.**—Glycosides comprise a widely distributed group of plant constituents which upon hydrolysis by enzymes or reagents yield one or more sugars among the products of the reaction. If the sugar formed is glucose, the substance may be called a *glucoside.* Since, however, other sugars besides glucose (*i. e.,* rhamnose) frequently occur the name *glycoside* seems preferable. The

non-sugar portion of the glycoside is called the *aglycon*. Both *alpha* and *beta* glycosides are possible as illustrated by the formulæ for methyl glycoside:



alpha methyl glycoside



beta methyl glycoside

It is interesting to note, however, that only beta forms occur in plants. This is evidenced by the fact that emulsin and other natural enzymes hydrolyze only the beta varieties.

From a biological viewpoint glycosides play an important rôle in the life of the plant involving its regulatory, protective and sanitary functions. Among such a wide variety of compounds one would expect to find many therapeutically active agents, and such is the case. In fact, the group contributes to almost every therapeutic class. Some of our most valuable cardiac specifics are glycosides from digitalis, strophanthus, squill, convallaria, apocynum, etc.; laxative drugs as senna, aloe, rhubarb, cascara sagrada and frangula contain emodin and other anthraquinone glycosides; sinigrin, a glycoside from black mustard, yields allyl isothiocyanate, a powerful local irritant, while gaultherin from wintergreen yields methyl salicylate, an analgesic. Many of the glycosides, such as strophanthin, salicin and digitoxin, have been isolated and purified, and employed in this form as medicinals.

The classification of glycosides is a difficult matter. If the classification is based on the sugar group a number of rare sugars are involved, the structures of which are not too well known; if the aglycon group is used as a basis of classification one encounters groups from probably all classes of plant constituents, tannins, sterols, carotenoids, anthocyanins and many others including several whose structures are as yet unknown. A therapeutic classification, while excellent from a pharmaceutical viewpoint. omits many glycosides of pharmacognostical interest. The classification on page 309 presents an attempt at a pharmacognostic-chemical arrangement.

3. **Tannins.**—Tannins are complex substances widely distributed in the plant kingdom. They are often associated with simple sugars and some of them may be glycosidic in character. They possess phenolic groups to which their action is due. Tannins precipitate proteins from solution and also have the property of combining with proteins rendering them resistant to proteolytic enzymes. This action when applied to living tissue is known as an "astringent action" and all drugs used as astringents depend upon their tannin content to produce this action. Many tannin drugs such as nutgall, krameria, gambir, kino, etc., as well as partially purified tannins (tannic acid) and their derivatives (acetyl tannic acid) are employed in medicine as astringents both to the gastro-intestinal tract and on skin abrasions. In industry tannin-bearing plants find extensive use in the manufacture of leather and ink.

Chemically tannins are complex substances which may be classified as to whether they yield catechol or pyrogallol upon decomposition. Their rôle in plant metabolism is somewhat speculative, but they probably serve as a protective to the plant during certain stages of growth, and are finally either destroyed or deposited as end products of metabolism in certain dead tissue of the mature plant. (See pages 213 to 215.)

4. **Fixed Oils, Fats and Waxes.**—Fixed oils, fats and waxes are esters of aliphatic acids. In fixed oils and fats the acids are of the fatty-acid series and the alcohol is glycerol. The fats and fixed oils are obtained from either plants or animals where their primary function is food (energy) storage. In either case there is evidence that they may be synthesized from carbohydrates. The fixed oils and fats are important products both pharmaceutically, industrially and as foods. Some, such as chaulmoogra oil, have special therapeutic properties. Waxes may also be of plant or animal origin. Many drugs contain fixed oils and fats as their principal constituents, and in not a few instances the fixed oils and fats are separated from the crude vegetable drugs (by expression) or the crude animal drugs (by rendering or extraction) and are employed as drugs in the refined state. (See page 394.)

Waxes are usually defined as esters resulting from the condensation of high-molecular weight, straight-chain acids and high-molecular weight, primary, straight-chain alcohols. Such esters, of course, exist in waxes, but in reality waxes are mixtures of different molecular weight acids and alcohols. In addition waxes may or may not contain paraffins. Waxes are found in plants in connection with the epidermal cells of fruits, leaves and other structures where the principal function seems to be protection against the penetration or loss of water. Insects also secrete waxes for various purposes. Caranuba wax (*Copernicia cerifera*) and bayberry wax are examples of vegetable waxes while lac wax and beeswax are examples of insect waxes. Waxes are employed in pharmaceuticals for "hardening" ointments and in the preparation of cerates. In industry and in the arts they are used for protective coatings. (See page 395.)

5. **Volatile Oils.**—Volatile oils are odoriferous principles found in various parts of plants. Since they are volatile with steam and usually immiscible with water they are called "volatile" or "essential" oils, ("essential" oils because they are the "essences" or active constituents of the plant parts). They differ from fixed oils in that they do not leave a permanent stain on filter paper, and do not consist of glyceryl esters of fatty acids, as do the fixed oils. In chemical constitution they vary widely and are mixtures in which almost any type of organic compound (hydrocarbons, alcohols, ketones, aldehydes, ethers, etc.) may be found. The most commonly occurring compounds, however, are terpenes, or their derivatives.

Volatile oils usually occur in specialized secretory structures such as glandular hairs (*Labiatæ*) or lysigenous or schizogenous passages (*Pinaceæ, Rutaceæ*), and these in turn are often localized in only one part of the plant. Many crude drugs are used because of their volatile oil content, and in many other cases the oils are separated by steam distillation and become drugs in themselves. Many volatile oil drugs are powdered and find extensive use as spices (pepper, clove, sage). The oils, or extracts of the drugs, are used as condiments. Thus, the most common use of volatile oil drugs as well as volatile oils is for flavoring purposes. They all possess a carminative action, and a few, such as oil of eucalyptus, possess additional therapeutic properties. In addition to their pharmaceutical use the volatile oils have a wide economic use in the flavoring of foods and confections and in the spice, perfume and cosmetic trades.

6. **Resins, Oleoresins, Gum-resins, Balsams and Balsamic Resins.**—Resins are more or less solid amorphous products of a complex chemical nature. They are usually formed in schizogenous or in schizolysigenous ducts or cavities and are end products of metabolism. Physically, they are usually hard, transparent or translucent and upon heating soften and finally melt. Chemically they are complex mixtures of resin acids, resin alcohols, resinotannols, esters and resenes. They are insoluble in water. Some investigators believe them to be oxidation products of the terpenes. Several resins are used in pharmacy and in the arts, among which rosin, guaiac and mastic are typical examples.

Resins often occur in more or less homogeneous mixtures with volatile oils. Such mixtures are known as oleoresins. Typical examples of pharmaceutical oleoresins are turpentine, Canada turpentine, copaiba and the oleoresins from aspidium, cubeb and capsicum. Resins also occur in mixtures with gums, from which the gums may be separated with water. Examples of gum-resins include asafetida, gamboge and myrrh.

Balsams are resinous mixtures that contain benzoic or cinnamic acids or both, or esters of these acids. Benzoin, balsam of Peru, tolu and storax are examples of balsams. The term "balsam" has been erroneously applied to some oleoresins in such terminology as Canada balsam, balsam of copaiba, etc. This error has occasionally led to some confusion.

In a few cases resins are found in glycosidal combinations, such combinations being called "glucoresins" or more properly "glycoresins." Such glycoresins are found in ipomea, jalap and podophyllum. The nomenclatures of these resinous combinations is at best only an artificial one, since it is often the case that small amounts of volatile oil will be present in gum-resins and small amounts of gum in oleoresins. (See page 103.)

7. **Alkaloids.**—Alkaloids are crystalline or oily compounds usually basic in character, found in plants. Many of them possess marked physiological action and some are highly toxic. Drugs containing them have been of dramatic interest to mankind for ages past. Even today, alkaloidal drugs are among our most valuable remedies, some of them such as quinine and eserine being specifics for certain diseases.

Plants yielding alkaloids are comparatively few in nature, in fact, it seems that their presence is confined to certain plant families. They may, however, occur in almost any plant part. The mode of their formation in plants is unknown, as is also their relation to the metabolism of the plant. All alkaloids contain one or more nitrogen atoms and are usually basic in character. They readily form salts with acids which are usually soluble in water, but insoluble in organic solvents. Since the free alkaloids are usually insoluble in water and soluble in organic solvents, this offers a ready means for their isolation, purification and estimation. The alkaloids may be classified according to their chemical constitution. (See pages 591 to 596.)

The physiological action of alkaloids varies widely; some like morphine and codeine are analgesics and hypnotics while others like caffeine are cerebral stimulants. Some like atropine are mydriatics while others like physostigmine are myotics; in fact the alkaloids cover a wide range of physiological actions.

Among the important drugs that contain alkaloids are ergot, belladonna, nux vomica, physostigma, cinchona, ipecac, hydrastis, coca, pilocarpus, opium and ephedra.

8. **Proteins.**—Proteins are nitrogenous organic substances produced by and associated with living matter. They occur in both plants and animals; those from plants being more easily isolated in crystalline form. Plants store proteins usually in the form of aleurone grains. In animals, proteins occur as living matter from which it is difficult to obtain them in the individual state.

Proteins are classified into three groups: simple, conjugated and derived. *The simple proteins hydrolyze entirely into amino acids; the conjugated* proteins are combinations of a protein and a non-protein group, the latter being called the prosthetic group and the derived proteins are degradation products of the proteins. Each of these groups has several subdivisions.

Proteins are of great importance in biochemistry (the chemistry of life) since they are present in all living matter. They also form an important class of food being equally as essential as carbohydrates and fats. Meat, fish and eggs are important protein foods. While proteins are of vast importance in metabolism they are only of passing interest as drugs. They are found as constituents in many drugs such as the glandular products but about the only drugs which might be definitely classified as protein drugs are gelatin and egg yolk, and these are strictly pharmaceutical necessities.

Many individuals are sensitive to certain proteins (allergy) and extracts of *proteins are used both in identifying causes of allergies as well as for purposes* of desensitization. Closely related to the simple proteins are the amino acids, which have recently been employed therapeutically in certain protein deficiencies.

9. **Enzymes.**—Enzymes are organic catalysts produced by living cells. They make possible most of the chemical reactions which make up life processes. Their chemical constitution is unknown but it is believed that most of them are proteins. Since they may be recovered and partially purified it would seem that they might be utilized as therapeutic agents as well as to control certain chemical reactions in industry. Pepsin, pancreatin and papain are employed therapeutically as digestants, while zymase and rennin find extensive commercial use in the fermentation and cheese industries. (See page 691.)

10. **Vitamins.**—Vitamins are organic compounds necessary to the normal growth and the maintenance of life in animals, including man. They act somewhat as enzymes during the metabolism of the energy-yielding food constituents. When the natural supply of vitamins is lacking a number of deficiency diseases occur. Vitamins are therefore therapeutic agents valuable in the prophylaxis as well as the cure of these diseases. Vitamins have a wide variety of sources, both plant and animal. They are usually isolated, concentrated and purified for use as drugs. They belong to no single chemical category and vary widely as to chemical constitution. Some are related to the sterols (vitamin D), some are relatively simple (niacin), while others are quite complex. Because of their importance a considerable amount of study has been given to their chemical constitution, and some have been prepared synthetically. An extensive discussion of vitamins will be found on pages 664 to 676.

11. **Hormones.**—Hormones are the active substances secreted by the endocrine glands. They control the growth, development and metabolism of the body in various ways. Like the vitamins they exhibit a variable chemical constitution. Some like ephedrine and thyroxin are simple basic compounds and amino acids, others like the pituitary and parathyroid hormones and insulin are peptid or peptone compounds, while still others like the sex hormones and those of the adrenal cortex are related to the sterols. The hormones are valuable therapeutic agents in treating conditions arising because of their natural deficiency. (See page 694.)

12. **Bacteriologics.**—This group includes a large variety of agents prepared from or by the action of bacteria and used in the prophylaxis and treatment of infective diseases. The group includes vaccines, immunogens, toxins, antitoxins and sera. Information concerning their chemistry is lacking, but they are probably protein in nature. They are relatively unstable and must be kept at low temperatures. They comprise an important group of biological, therapeutic agents. (See page 66.)

13. **Antibiotics.**—Certain molds and fungi synthesize compounds that are bacteriostatic and have been found exceedingly useful in treating diseases caused by bacteria and other microörganisms. Representatives of the group are penicillin and streptomycin. They have received a great deal of chemical investigation and while their constitution has not been definitely established, it may soon be. They appear to be mixtures of related compounds. (See page 78.)

14. **Sterols.**—Sterols should probably be classified next to the fixed oils and fats since they occur commonly in the unsaponifiable portions of fixed oils and fats. They have, however, been placed last since many compounds classified in other groups are related to them. Among these are some of the vitamins (vitamin D), the estrogens, the androgens, the adrenal cortex hormones, the digitalis aglycones, the saponin glycosides and cholesterol. The sterol nucleus is therefore an important one in the chemistry of drugs. (See page 685.)

Not all vegetable and animal drugs can as yet be classified in the above scheme, but as our knowledge of their chemistry increases their place in the arrangement will be established. Since it is these chemical entities in vegetable and animal drugs that exert their physiologic action, it would seem that such a chemical arrangement would be the most logical one for the study of these drugs.

INSPECTION AND ANALYSIS OF VEGETABLE AND ANIMAL DRUGS

(Analytical Pharmacognosy)

Drugs are inspected by pharmaceutical manufacturers before purchase for economic reasons, and after purchase, to insure the high standard of the materials to be used in their products. Various state and municipal agencies also maintain laboratories for the inspection of drugs, largely in connection with their health and sanitation measures. The Food and Drug Administration operating under the Federal Security Agency conducts a nation-wide inspection service. It maintains, in addition to its principal laboratory in Washington, several District Laboratories in the major cities of the United States. These laboratories are administered as three districts, the Eastern, Central and Western. The Administration is mainly concerned with drugs in interstate commerce and with all imports into the United States. It maintains a large corps of inspectors in the field, and an additional group associated with the custom's officers at the ports of entry. Samples are taken, sealed and sent to the central laboratory at Washington or to the nearest district laboratory where they are examined by microanalysts.

As was mentioned before, the standards set forth in the monographs of the U. S. Pharmacopœia and the National Formulary comprise the legal standards for the drug. In sampling, the directions of the U. S. P. and N. F. are followed. Cores are taken from bales and other bulk packages and the scheduled number of packages are taken from small-package lots.

The analyst first determines whether the sample conforms to the macroscopic and microscopic descriptions in the official monograph, noting especially the descriptive morphological features, the size, color, etc. Where necessary he prepares sections and checks with the histological descriptions in the monograph. He also determines the amount of foreign organic matter by the U. S. P. or N. F. method. This method involves simple hand separation and requires that the analyst be well trained in the identification of foreign organic matter.

A representative sample of the original sample is then taken, and if the drug under examination be a whole drug, the sample is reduced to a powder that will pass through a No. 20 sieve. This sample may be further reduced by quartering, and is employed for the subsequent examination.

The total ash and acid-insoluble ash are determined by the official method. In brief this consists of incinerating and weighing the total ash; then boiling the total ash with dilute hydrochloric acid, filtering, igniting and weighing the acid-insoluble ash. Acid-insoluble ash consists of sand, silicates, etc., and is an indication of the amount of dirt, soil, clay, and so on, present in the sample. It is sometimes called "foreign inorganic matter."

Moisture, if in excess, is considered an adulterant because of its added weight as well as the fact that excess moisture is conductive to the promotion of mold and bacterial growth, and subsequently to deterioration and spoilage of the drug. Moisture up to 5 per cent is usually not considered excessive. It is usually determined in one of two ways. If the drug contains no volatile material, a weighed sample is heated at 100° C. to constant weight, the loss in weight being the moisture content. If, however, volatile constituents are present, these must first be determined by the volatile ether extractive method, and their weight deducted from the loss in weight upon drying, before the moisture content can be determined. A second method is by means of toluene distillation,

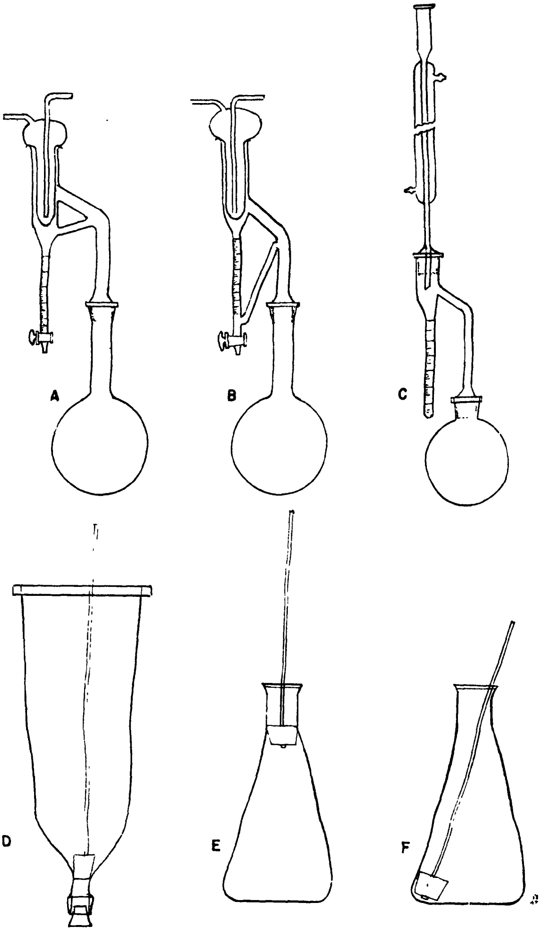


FIG. 13.—*A, Clevenger apparatus for the determination of volatile oils heavier than water.* The flask is charged with a quantity of drug that will yield from 1 to 2 cc. of volatile oil and enough water is added to fill the flask about three-fourths full. The trap is then connected to the flask and the flask immersed in an oil bath. The trap is then filled with distilled water and the pear-condenser inserted. The oil bath is maintained at a suitable temperature (125° to 135° C.) to insure gentle boiling of the contents of the flask. Steam carrying the volatile oil rises through the neck of the flask, both being condensed on the surface of the pear-condenser. The oil being heavier than the water sinks to the bottom of the trap and is determined volumetrically. The condensed water returns to the flask through the side-arm, the process thus being a continuous one. Between two and four hours is usually sufficient to remove all of the oil from the drug. *B, Clevenger apparatus for the determination of volatile oils lighter than water.* The flask is charged and the operation carried out as before. In this case, however, the oil floats on the water in the trap, and is again determined volumetrically. After the determination, in either case, the oil may be removed through the stop-cock at the bottom of the trap and its optical and other constants determined. *C, Toluene moisture apparatus.* The dried flask is charged with a quantity of drug that will yield between 2 and 4 cc. of water. About 200 cc. of toluene are added and the trap and condenser connected, after which the trap is filled with toluene. The flask is heated on an electric heater or an oil bath: the toluene and water distill over; the water being heavier sinks to the bottom of the trap and the toluene returns to the flask. At the end of the distillation, after the apparatus has cooled, the collected water is determined volumetrically. *D, Percolator for the separation of filth by sedimentation.* The lower cork is inserted into the bottom of the stem of the percolator and the percolator

and is applicable in either case. In this method the water is distilled from the drug with toluene in a continuous distillation apparatus, the water being caught in a trap and determined by volume. (See Fig. 13.)

Quality standards depending upon the amount of principles capable of being extracted, have been devised for certain drugs. The drug is extracted usually in a continuous extraction apparatus of the Soxhlett type, and the extract determined by weight after removal of the solvent. The common solvents used are alcohol, diluted alcohol, petroleum benzin, ether and water.

FIG. 14.—Root of a rodent hair. Rodents frequently lick their fur and it is not uncommon to find hairs in the pellets. Such hair bases are identity characteristics of rat and mouse pellets. (Photograph by Paul D. Carpenter).

The amount of volatile oil in volatile oil-containing drugs may be determined by distillation. In this method the drug is distilled with water in the proper Clevenger apparatus. This is a continuous distillation apparatus in which the separated volatile oil is caught in a trap and determined by volume. (See Fig. 13.) In an older and less accurate method the drug is extracted with ether, the solvent removed by evaporation and the moisture by desiccation, after which the volatile oil content is determined by the loss in weight upon heating to 110° C.

LEGEND OF FIG. 13.—CONTINUED

filled about two-thirds full with chloroform (sp. gr. about 1.48). The sample is then added, vigorously stirred and allowed to separate. Cereals for example will float while rodent pellets will sink into the stem of the percolator. The cork fastened to the metal rod is then inserted from above as illustrated, trapping the filth between the corks. The filth may be recovered for microscopic examination by removing the lower cork. *E*, *F*, *Wildman trap flasks for the recovery of filth by flotation.* A leaf drug, for example is placed in the flask, *F*, and boiled with water. After cooling the flask is filled nearly to the neck with water and 25 to 50 cc. of gasoline or mineral oil are vigorously stirred into the mixture using the metal rod attached to the rubber stopper as a stirring rod. After separation enough water is added to bring the oily layer into the neck of the flask. By raising the rubber stopper attached to the metal rod to the position indicated in *E*, the oily layer containing insects, insect parts, rodent hairs, etc., can be easily removed for microscopic examination. (Drawing by E. H. Wirth.)

Alkaloids are recovered from the drug material by extraction. After purification with immiscible solvents the alkaloid may be determined gravimetrically, or volumetrically by titration of the amount of acid necessary to convert it into a salt.

In a few cases, special assays for drugs containing some definite chemical constituent have been devised. In others where no chemical, physical or extractive assay is known the quality is determined by a bioassay.

After performing any additional special tests for purity or foreign matter as well as for quality, the analyst is able to prepare his report concerning the drug in relation to its conforming to the standards of the U. S. P. or N. F. *monograph.*

The Food and Drug Administration is very particular concerning conditions under which the drugs have been produced, transported and stored. Excessive moisture may cause decomposition and improper protection from insect or rodent attack may render the drug filthy and unfit for use. The Administration has devised special methods for the separation and identification of manure, rodent feces, rodent hairs and other filth, as well as for the separation and identification of insects. These methods are published in Food and Drug Circular No. 1, "Microanalysis of Food and Drug Products." Field insects in minute amounts are inavoidable but storage insects indicate careless handling and storage, often with the accompanying destruction of the drug. Any evidence of rodent damage such as rodent hairs, feces or urine is inexcusable and indicates gross negligence in the storage and protection of the drugs. Not only is insect and rodent damage objectionable from the purely esthetic point of view; it may render the drug dangerous and certainly renders it unfit for human consumption.

Insects, insect parts, rodent hairs and feces may be separated from the drug by means of liquids of varying specific gravities. Most drug material will float on, for example, chloroform, but rodent pellets will sink in this liquid. Insect parts can be separated by boiling the drug with water cooling and then vigorously stirring in a small amount of mineral oil. The mineral oil rises to the top carrying with it the chitinous insect fragments. Floating strata may be separated by means of the Wildman trap flask and sinking strata by means of a percolator equipped with two corks at either end of the stem. (See Fig. 13.) The recovered impurities are then identified microscopically. Food and Drug Circular No. 1 contains several variations of these gravity separation methods applicable to specific cases and also presents several illustrations useful in identifying insects and insect parts.

The following few illustrations from the weekly reports of detentions at the Port of New York in 1946, illustrate types of frequent and common adulteration as well as the terminology used in reporting such adulteration.

Product	*Quantity*	*Reason for detention*
Juniper berries	130 bags	Filthy
Cassia	113 bags	Insect infested
Nutmegs	47 bags	Wormy and moldy
Cassia oil	10 drums	Contains rosin and heavy metals
Areca nuts	240 bags	Moldy
Aconite root	20 bags	Excess stems
Angelica root	17 bales	Excess acid-insoluble ash
Cassia oil	9 drums	Not U. S. P.
Senna leaves	96 bales	Filthy—excess foreign organic matter
Olive oil	4 drums	Rancid
Orris root	112 bags	Insect bored
Colombo root	210 bags	Wormy
Coriander seed	381 bags	*Live insects*
Amyris oil	1 drum	Not N. F.

Product	*Quantity*	*Reason for detention*
Cumin seed	312 bags	Filthy—oil damaged
Henbane	172 bales	Egyptian henbane—not the official variety
Safflower	22 bags	Rodent excreta
Digitalis	39 drums	Filthy—excess foreign organic matter
Stramonium leaves	23 bales	Manure and rodent filth
Buckthorn bark	54 bales	Not N. F.
Cod oil	100 drums	Decomposed
Aconite root	*6 bags*	*Excess moisture*
Thyme leaves	220 bags	Not official variety
Juniper berries	88 bags	Excess immature and discolored berries
Shelled almonds	122 bags	Water damaged
Almonds (shelled)	47 bags	Dirty—excess bitter almonds
Ginger peelings	57 bags	Valuable constituent abstracted

THE CULTIVATION OF DRUG PLANTS

The cultivation of drug plants is advantageous in that botanical source and purity can be controlled. Drugs of superior quality can be produced by breeding, control of disease, proper harvesting and drying. If operations are to be profitable a number of factors must be considered, including land and labor costs, investments in equipment and the cost of fertilizers, insecticides, seeds or planting stock, etc. The production of drug plants is a horticultural process and so involves a knowledge of propagation, cultivation, soils and the many factors affecting plant growth. Since climatic conditions vary widely and since each species has its own particular problems and habits, no more than a general outline of the principles involved can be given. It is the intention of the following discussion to present to the student such an outline so that he may have some conception of the factors involved in the cultivation of drug plants.

Propagation.—A number of plants can be grown from seed, but others are best propagated by vegetative means.

Seeds of the better-known varieties of medicinal plants are listed in the catalogs of numerous seed houses. Seeds less commonly known and not listed can usually be obtained from dealers who make a specialty of handling one or more of these species. In ordering, it is preferable to specify by using the botanical names rather than the common horticultural names. This lessens the possibility of obtaining related horticultural varieties which may possess very little or no medicinal value.

All seeds should be tested as to their viability and longevity by germination tests. Some seeds naturally sown at the season when they ripen will not germinate if kept until spring sowing. Other seeds require a period of dormancy. The germination of seeds may be hastened prior to sowing by several methods, such as soaking them in water, or treating them with various chemicals of different strengths and for varied periods. Other special methods involve stratification, alternate freezing and thawing, scratching, cracking or "clipping" the seed coat.

Several of the medicinal plants can be satisfactorily grown from seed sown in the field; with others because of climatic conditions or short summer seasons, sowings should be made in seed-flats or seed-pots, or in a greenhouse bench, hotbed or cold frame. When plants started in this manner are placed in the

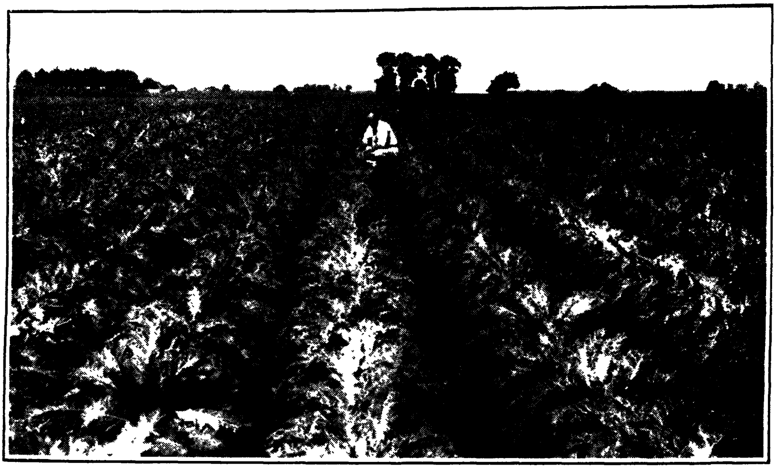


FIG. 15.—Test field of first year plants of *Hyoscyamus niger*. University of Illinois Drug Plant Experiment Station.

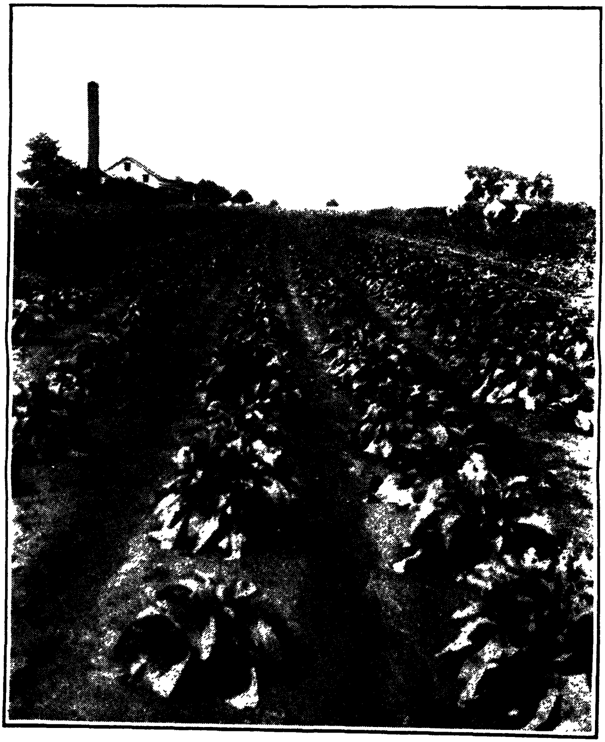


FIG. 16.—Test field of first year plants of *Digitalis purpurea*. University of Illinois Drug Plant Experiment Station.

field they will show an increased yield, will be able to overcome attack of disease and insects and perhaps reach maturity earlier.

Preparation of the soil for the seedbed is most important. Equal parts of clean sand, garden soil, well rotted manure, and leaf mold, the coarse material finely subdivided, and thoroughly mixed is a suitable medium. The character of the soil may be governed by the addition of lesser or larger amounts of sand depending upon the garden soil used. The final mixture should not be too

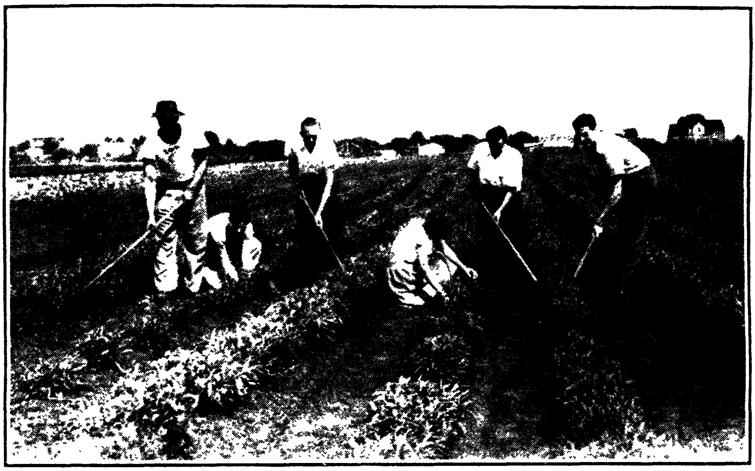


Fig. 17.—Students hand cultivating sage. University of Illinois Drug Plant Experiment Station.

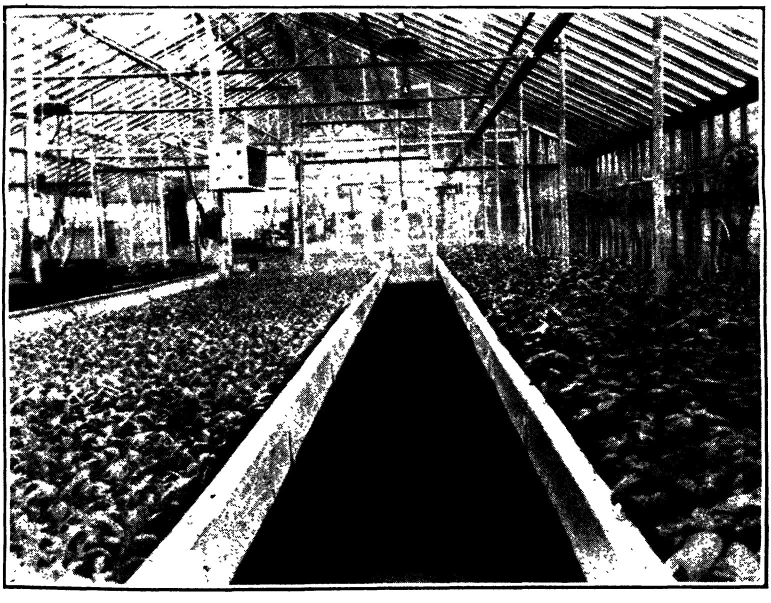


Fig. 18.—Seedlings in greenhouse benches before transfer to the field. University of Illinois Drug Plant Experiment Station.

heavy, soggy nor too coarse in texture. Before sowing, this soil should be thoroughly sterilized with steam or formaldehyde. If formaldehyde is used, care must be taken that the soil is well aerated before sowing as formaldehyde is very toxic to young plants. Sphagnum moss and vermiculite are also considered good for seedbeds.

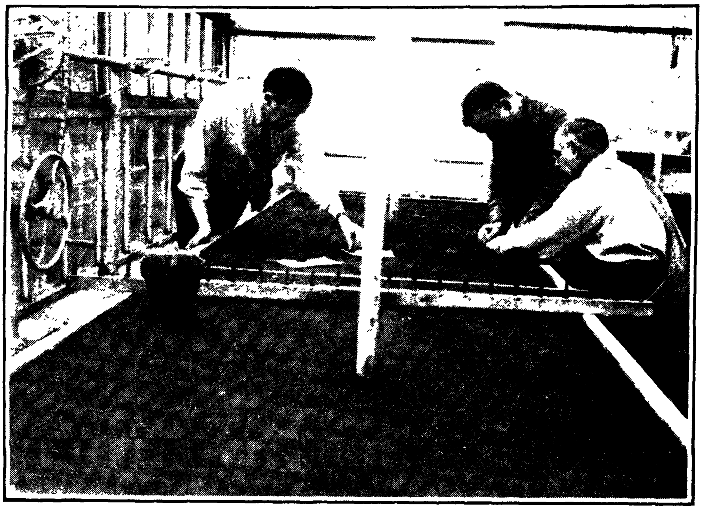


FIG. 19.—Transplanting seedlings to the greenhouse bench. University of Illinois Drug Plant Experiment Station.

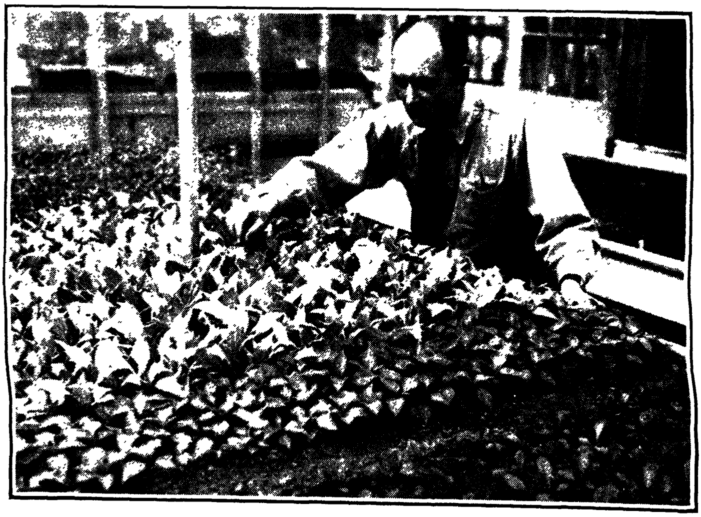


FIG. 20.—Inspecting seedlings in the greenhouse bench. University of Illinois Drug Plant Experiment Station.

Depth of sowing is governed by the size of the seeds and the character of the soil. As a general rule the seed should be planted at a depth about equal to their diameter, and should be covered more deeply in a light soil than in a heavy.

The amount to be sown depends upon the germination of the seed, and the number of plants required for a given area of land. It is usually advisable to sow seed in considerable excess of the amount needed to cover unpredicted losses such as transplanting fatalities, loss from insects and disease attacks.

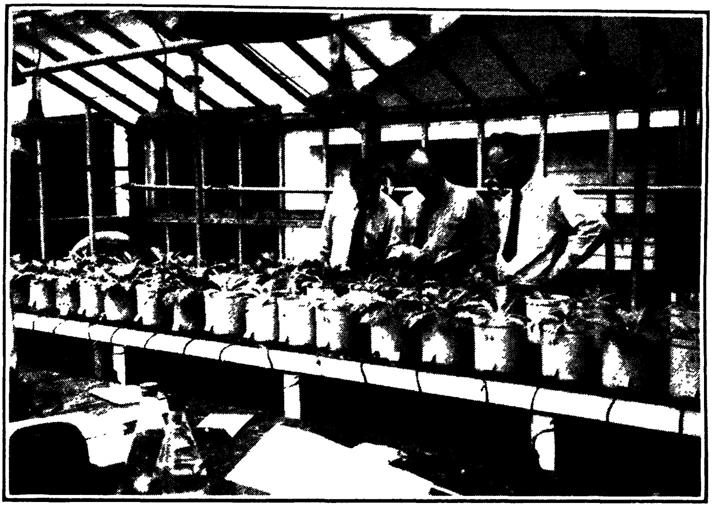


FIG. 21.—Hydrophonic test with *Hyoscyamus niger*. Hydrophonics offers a means of testing the nutrient factors necessary to plants. University of Illinois Drug Plant Experiment Station.

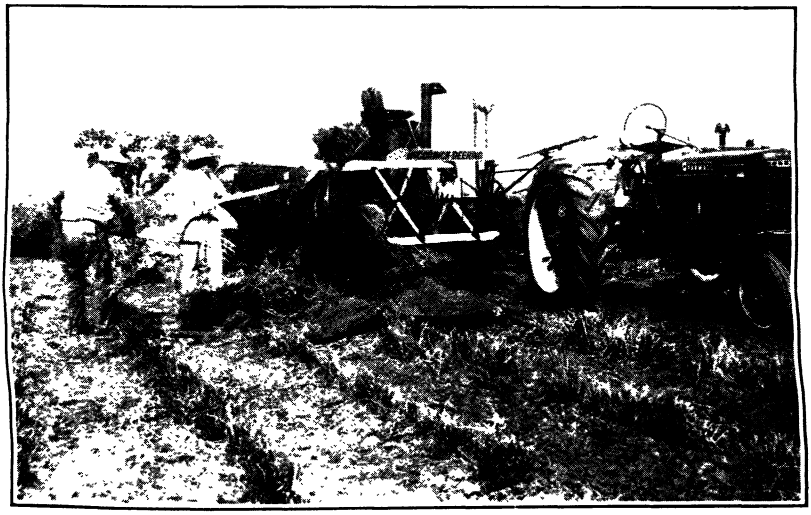


FIG. 22.—Threshing caraway seed. University of Illinois Drug Plant Experiment Station.

Prior to sowing the seed in the open field, the soil should be specially preared by freshly disking the plowed field, and then meeker-harrowing it until he soil is as finely subdivided as possible. The seed is preferably placed in rows with a seed drill rather than sown by hand. With the drill, the depth of sowing is more uniform and the soil is compacted over the seeds, thus favoring better germination. The distance between the rows depends upon the size of plants at maturity and the method of cultivation to be used. Eighteen inches to three feet is the common range.

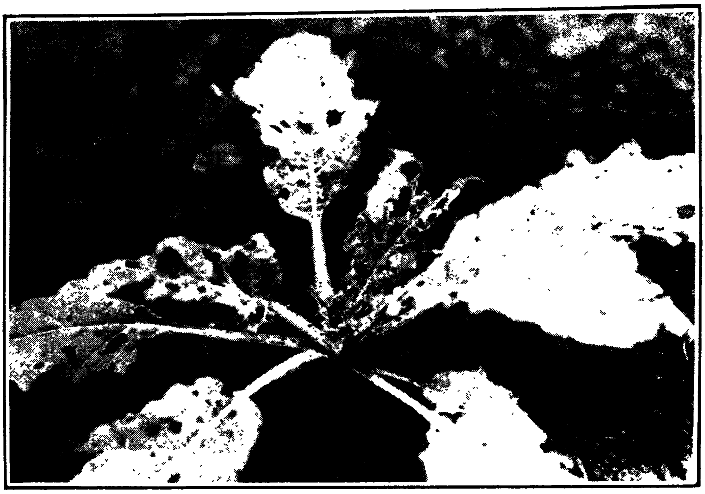


FIG. 23.—Damage to young plant of *Hyoscyamus niger* by the Colorado potato beetle. University of Illinois Drug Plant Experiment Station.

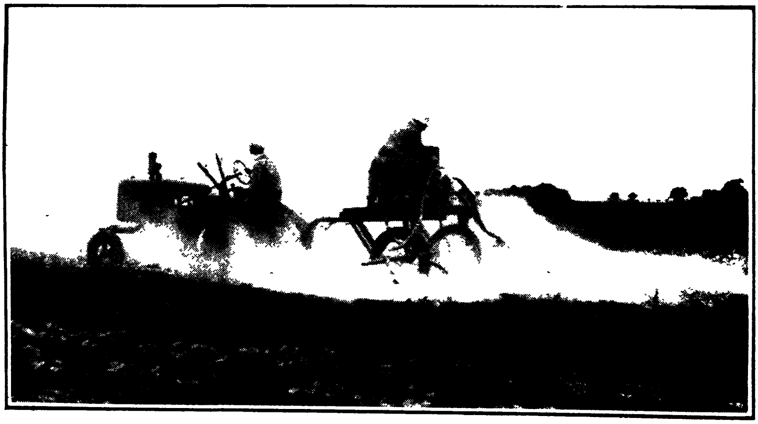


FIG. 24.—Dusting with rotenone dust to control the Colorado potato beetle. University of Illinois Drug Plant Experiment Station.

When the seedlings have reached a height of 1 inch or more and have produced one or two true leaves, they are ready for transplanting. This operation is a severe shock to the plant and interferes with its activities because the soil is loosened and many of the roots are destroyed. The top continues to transpire moisture which produces a drying effect on the plant. The transplanted plant should therefore be well supplied with moisture and made firm so it will soon reëstablish its root system. Transplanting is most successful on an overcast, cool, cloudy or foggy, damp day and the younger the plant, the better are its chances for recovery.

The plants may be transferred into regular clay pots, the ordinary paper pot, into regular flats, or placed directly into the soil of the greenhouse benches. The regular flats are shallow wooden boxes, 3 inches deep, 12 to 14 inches in width and 14 to 18 inches long. The seedlings when placed in either the flats or greenhouse bench are spaced in rows, about 2½ or 3 inches apart each way. When individual plants have more space they develop stocky and healthy overground parts and also better root systems. These plants will be better adapted for later transplanting to the field. The soil into which these plants are placed should have been previously sterilized, and it should be rich and of approximately the same character as that in the field to which they will be finally transplanted.

Plants may be transferred to the field as soon as they can be safely grown out of doors. Some may be placed in the field at an earlier date than others because of their natural hardiness toward cold weather or frosts. The requirements and necessary care for each plant are best determined by experience and observing the growth habits of each.

Prior to field planting, the soil must be well prepared by proper plowing either in the fall or spring, followed by repeated disking and meeker-harrowing until all soil particles are finely subdivided. If it is only a small area of about an acre or two, it may be properly prepared by using a roto-tiller. If the soil requires a fertilizer it should be incorporated while preparing the soil.

Transplanting by hand is a laborious process and is the only alternative for small plots. For larger areas which will allow space at the ends for wheel machinery, a mechanical transplanter is the most suitable labor and time-saving device. The planter digs a furrow, the plant is set in place accompanied with ample water and the dirt is firmly pressed around it. If the planting must be done in hot weather, the plants will recover best if shaded with a shingle or flat board. The plants should be set at such distances as to insure best growth and at the same time permit the use of cultivators and other agricultural machinery.

During field growth, frequent cultivation and weeding must be carried on. Excessive growth of weeds tends to lower the available moisture and nutrients for the desirable plants. Cultivation with either the hoe or cultivator at frequent intervals also tends to prevent caking, loss of moisture and aerates the soil. A well cultivated soil will lose less moisture during a dry hot season.

The plants must be inspected for insect and plant disease attacks. These barriers to plant growth may be controlled by means of sprays and dusts. Chemicals such as arsenic or other known harmful substances cannot be used because they will adhere to the plant and be carried over into the drug or its preparations.

Vegetative propagation consists of the production of a complete plant from a bud. Asexual reproduction of plants differs from sexual reproduction in that vegetative plant parts such as stems, roots, bulbs and leaves are used rather than seeds. It is a method whereby varieties may be reproduced and preserved indefinitely and is a process of isolating superior strains of varieties and preserving them true to type. The methods by which plants may be reproduced asexually are division, layerage, cuttage and graftage. The particular process to be followed should be determined by the adaptation of the plant to be reproduced. Plants propagated by one method do not differ in any basic respect from those that may be propagated by another, and the simplest method that will give satisfactory results is always used.

Division is applied to the separation of a plant which has a number of aerial stems or buds into separate parts each having roots and a growing point. In division they do not naturally break apart but may be cut or torn from the plant before rooting. Some parts often detach themselves into new plants, such as bulbs and corms.

Layerage is used in the propagation of plants that do not come true to type when grown from seed; that do not form offshoots or specialized buds which may be used, and also for plants that do not graft readily and whose stems or leaves do not root easily when made into cuttings. It is a method of inducing rooting by bending the stem until its tip touches the ground and then covering the tip with a little soil. It begins to thicken, take root and establish a new plant. Stems that form roots while still attached to the parent plant are called layers. When long shoots are alternately covered and exposed over their entire length the process is known as compound layerage. An advantage of layerage is that it does not require the close attention required by cuttings and the disadvantages are, that it is a slow and cumbersome method of propagation and may interfere with cultivation.

Cuttage is the process of propagation using such plant parts as roots, rhizomes, tubers, stems or leaves, which are cut in pieces with or without buds. These pieces take root and asexually produce new plants of the same variety and species as the parent plant. It differs from layerage in that the parts used are detached from the parent plant before they have an opportunity to develop roots. Propagation by cuttings is a cheap, convenient and popular method to secure new plants. A fully developed and often stronger plant is obtained in less time than when seed is sown, and the character of the variety is preserved in the new plant.

Graftage is the art of inserting a part of one plant into another plant usually different but closely related, in such a way that the two will unite and continue to grow together. The rooted plant is called the stock and the portion cut off *is the scion or graft. It differs from cuttage, layerage and bulb propagation in that the plant part expected to produce the top of the new plant is deprived of* its own root system and unites with another plant that supplies this part. Graftage is a means of preserving and perpetuating some varieties that cannot be reproduced easily by other vegetative methods and it is also used to alter certain plant characters.

The requirements and necessary care toward plants produced by one of the above vegetative processes is the same as for any plant grown from seed. The same cultural practices such as transplanting and cultivation preparations are observed.

Factors Affecting Cultivation.—*From the time the plant is placed in the field until it is harvested*, a number of factors may favorably or unfavorably affect its growth. Climate, soil, management of the soil, fertilizers and plant disorders are a few of the important factors to be observed and considered.

Climate.—Plant growth is definitely affected by climate. All of the climatic factors are interrelated whereby an excess or a deficiency in one factor may limit the effect of the other factors of climate.

Conditions of temperature that are the most favorable for growth of one kind of plant or for one growth process may not be most favorable for that of some other plant or growth process. Minimum and maximum temperatures that a plant will endure may be much lower or higher than that which another will tolerate. Different parts of the same plant vary greatly in the temperature that they will endure, depending on the season of the year and condition of maturity. The grower should know the temperature range for a given growing area and likewise know the approximate temperature that his plants will withstand at different stages of growth.

Classification of crop plants is based upon temperature relations and are most commonly divided into temperate, subtropical and tropical zones. Temperature also regulates the length of growing seasons, and indirectly influences the prevalence of insects, fungi, bacteria and other parasites. It is possible for the grower to make many adjustments to temperature conditions through various cultural practices such as providing natural or artificial protection for *the plants when necessary, selection of type and variety of plant adaptable to* the growing area, and many other thoughtful considerations beneficial to the plant.

Water is the second important factor in plant growth. Since the amount of rainfall and degree of humidity regulates the availability of water to the plant, *the grower must regulate his plans according to this factor, in any given climatic* area. He will also be able to conserve much of nature's water supply by certain *cultural practices such as cultivation and mulching plus principles of soil conservation.*

Velocity of the wind influences evaporation of moisture from the soil, the strength of the plant, and in many cases flower fertilization. In some cases wind protection is necessary and is afforded by planting shelter beds or wind rows for the benefit of other plants.

Plants vary in the amount and intensity of light which they require. In certain cases light governs the amount of the principal constituent produced in the plant. Intensity of light and daily light period also affects the ability of plants to flower and reproduce. The native plant is found in places most suitable to its light requirements and therefore similar conditions should be supplied when cultivating that same plant.

Altitude directly or indirectly affects the presence of constituents in many plants. Some plants grow very luxuriantly at low levels but have no medicinal value unless grown at high elevations. Other medicinal plants are most adaptable to near-sea levels.

Soil is the product resulting from the various stages of disintegration and decay of rocks and plant and animal materials, in which plants can grow. The resulting product varies widely in physical, chemical and biological characteristics and consequently in its ability to support plant growth.

Physical Condition of the Soil.—*The physical condition of the soil is determined by texture and structure. Texture refers to the size of the individual soil particles and structure refers to the arrangement of the soil particles within a given soil mass. Sand, silt and clay are the principal soil groups which are separated into particles of different sizes as follows:*

Coarse gravel rock	more than 20 mm.
Fine gravel	20–2 mm.
Coarse sand	2–0.2 mm.
Fine sand	0.2–0.02 mm.
Coarse clay or silt	*0.02–0.002 mm.*
Fine clay or colloidal clay	*less than 0.002 mm.*

Class names such as sandy loam, loam, silt loam and clay give some idea of the textural make-up and structure of soils. Each class contains various proportions of different-sized particles.

	Per cent sand	*Per cent silt*	*Per cent clay*
Sandy loam	75	14	11
Loam	32	45	23
Silt loam	5	82	13
Clay	10	45	45

Porosity of soils is dependent upon the above classes. A light-textured soil consists of sandy soils and sandy loams and consequently is very porous. Loam and silt-loam soils which are medium textured are widely adaptable, while the heavy soils such as clay and clay-loam classes possess certain disadvantages in porosity.

Soil Fertility.—Fertility of the soil is an indication of its ability to support plant life when provided with the optimum conditions of light, moisture and temperature. A continuous interaction of physical, chemical and biological *forces, neither one independent of the other, determines soil ferility.* The degree of fertility of the soil also varies with the kind of plant growing on it, and the type of plant that can grow on it depends upon the fertility. Factors affecting soil fertility are soil, temperature, moisture supply, soil aeration, soil texture, organic supply, presence and availability of plant nutrients, the kind and *amount and activity of soil organisms, and soil reaction. All of these factors* are very important because each one is dependent upon the others in providing suitable soil conditions for plant growth. There is a direct and marked relationship between the soil properties and the growth of the plant.

Soil Topography.—Topographical variations must be considered because certain conditions are more suitable than others for the satisfactory and economic production of crops; because of different cultural operations and because of the influence of necessary tillage practices to control soil erosion. The position of the soil, that is, its aspect and elevation affects the temperature, water supply, the composition, the soil reaction and the content of soluble matter.

Soil Management.—Proper management of the soil is an intricate problem and therefore when judiciously exercised, it will favorably affect the cultivation of medicinal plants. The principal objects are to provide a favorable moisture supply; to supply sufficient nutrients for optimum growth and production; to add enough organic matter to offset that lost by decomposition, by organisms and by erosion; to prevent erosion; and to avoid injurious compacting of the soil. A good system of soil management which will satisfy these objectives includes five major features. The first of these is good tilth whereby plowing and cultivation conditions the soil physically for proper moisture, drainage and aeration requirements. Control of weeds is closely associated with good tilth. Third, plant diseases and insect pests are controlled by handling the soil in various ways. Fourth, a proper rotation of crops influences the soil physically, chemically and biologically. The fifth major requisite is to provide adequate supply of available plant nutrients by the use of good tilth practices, or by the application of fertilizers.

The primary interest of soil management is to maintain soil productivity and to commercially produce satisfactory plants and plant products at a minimum cost.

Fertilizers.—The use of fertilizers may favorably affect the production of vegetable drugs in quantity and quality. Soils in which plants grow are not alike in fertility while the plants themselves are not alike in their need for and use of nutrients in the soil. Sometimes fertilization is necessary and profitable but it can be definitely unnecessary and unprofitable at other times. Addition of plant nutrients to the soil is made to supplement the constituents present rather than to constitute the only source of supply. The application of a commercial fertilizer should be such that it establishes a proper balance between the necessary elements of nutrition. This balance is important in order to avoid an under- or overstimulation of the plants. Another factor to consider when applying commercial fertilizers is the amount of plant nutrients consumed by many of the soil microörganisms.

Nitrogen, phosphorus and potassium are often referred to as the fertilizer elements. Other elements of lesser importance are calcium, magnesium, sodium, iron, manganese, boron, copper, zinc, cobalt, molybdenum and aluminum. These are occasionally applied when certain plants by their symptoms demonstrate specific deficiencies of one or several of these elements.

Farm manure as an important agricultural by-product is a valuable fertilizer. It contains favorable microörganisms which aid in decomposing the organic matter in the soil and liberating plant food elements and adds humus to the soil which improves the physical condition. Green-manuring refers to the practice of turning into the soil undecomposed green plant tissue. This also brings about a number of favorable effects, and especially an increased organic matter content of the soil.

It is best to first determine the fertilizer needs and then exercise special care in the purchase and application of commercial fertilizers. Their misuse will quickly affect plant growth.

Plant Disorders.—Plants should be protected from all possible injury, in order to be productive. Any disorder, whether it be caused by insects, fungi, bacteria, viruses or because of some unfavorable environmental factor incapacitates a plant. In order to minimize the losses it is important to be on the watch for these disorders and injuries, to immediately ascertain the cause and apply the most efficacious remedial control measure.

When possible select an insecticide or a fungicide most specific for the parasite. Choose such agents that will not be poisonous to humans because they may be easily carried on the overground parts and found in the finished drug products.

Constitutional or physiological disorders due to environmental factors may be remedied by recognizing the cause and correcting the detrimental factor or factors. Many of the mechanical injuries such as bruises tend to heal over, causing more or less a scarring and malformation.

Preventive control measures are very effective. A legal means is to quarantine or apply special laws governing rigid inspection and transportation of plants. Isolation of the healthy plants and eradication of the infested material is helpful. Crop rotation, pruning, and certain soil cultivation practices will prevent further infestation. All propagating structures, equipment and greenhouse soils should be thoroughly fumigated or suitably sterilized.

A natural means of preventive control includes the development of varieties specifically resistant and immune to disease. Another method is to introduce competitive insects, fungi and bacteria that are harmless to plants but will destroy the detrimental organisms. In some cases a change in environment for the growing of certain plants would naturally control the attacks by plant pests because their growth and development depends upon a limited range of environmental factors.

THALLOPHYTA OR THALLOPHYTES

THE thallophytes comprise about 100,000 species of algæ, fungi and lichens, yet relatively few are at present of economic importance. The algæ are chiefly used as a source of iodine and for the mucilage that they contain, such as algin, carageenin and agar. A number of lichens yield important coloring matters used in pharmacy. Some of the fungi produce important medicinal agents, such as the antibiotics; others cause diseases in plants, animals and man.

SCHIZOMYCETES OR BACTERIA

The bacteria have been included in the past with the fungi, but now are generally considered as a separate group possessing both animal and plant characteristics. Hence, these organisms may be regarded as a connecting link between plants and animals.

Bacteria are non-chlorophyll-bearing, unicellular organisms, rarely more than 25 by 3.5 microns in size and may be as small as 0.5 by 0.2 microns. They possess an abundance of nuclear material but no true nuclei, and generally divide by transverse fission (*schizo* means to cleave or split; *myces* refers to fungus). In shape they vary from perfect spheres to greatly elongated rods, sometimes curved. Some rod-shaped species are motile by means of flagella, and some produce very resistant structures known as endospores. Of the several thousand species of bacteria, only a few have the power to infect animals or plants and thus produce disease.

Certain biological preparations of bacteria and of molds are valuable as specific cures for certain diseases or in prophylaxis and diagnosis. The production of these preparations requires special facilities and special care to prevent contamination, hence their manufacture is permitted only under government license and inspection. These products may be classed as Vaccines, Tuberculins, Toxins, Antitoxic Serums, Antibacterial Serums, Antibiotic Agents, etc.

These preparations should be preserved at a temperature between 2° and 10°C, preferably at the lower limit. They should be dispensed in the unopened glass containers in which they were placed by the manufacturers. To provide for a certain degree of deterioration, manufacturers package a product of higher potency than is stated on the label, and place a limiting date on the label after which the potency of the product is not guaranteed.

VACCINES

Vaccines contain attenuated or modified viruses, killed rickettsiæ or attenuated or killed pathogenic microörganisms (antibacterial vaccines), and are to be used as an inoculation to stimulate the production of antibodies, and thereby an immunity against the disease in its more virulent form. The general action of vaccines is therefore preventive (prophylactic). Some are used, however, as therapeutic agents.

The attenuation of viruses, or of pathogenic bacteria, so that they may be injected into the animal body without danger of producing serious pathological conditions, may be accomplished by one of the following methods: passage through some species other than the animal for which the infection is specific (smallpox vaccine); drying at constant temperature (rabies vaccine, Pasteur); growth at a temperature above the optimum (blackleg vaccine, anthrax vaccine); heating at a relatively high temperature (blackleg vaccine); and treatment with chemicals (anthrax vaccine).

Rabies Vaccine, Antirabic Vaccine or Pasteur Treatment (U. S. P. 1936 to date) is an uncontaminated suspension of the attenuated, diluted, dried or dead, fixed virus of rabies. The virus is contained in the tissue of the central nervous system of an animal suffering from fixed virus rabies infection.

This vaccine is solely for preventing development of rabies in persons bitten by an animal supposed or known to be rabid, and to be effective it should be administered as soon as possible after the wound has been inflicted. With the living vaccine, the ffrst dose is much attenuated and each succeding dose is less so until the last doses given are rather virulent. One dose is to be given daily up to a total of 14 to 21 doses. Each dose tends to build up the resistance of the patient against the disease.

Smallpox Vaccine, Glycerinated Vaccine Virus, Jennerian Vaccine (U. S. P. 1916 to date) consists of a glycerinated suspension of the vesicles of vaccinia or cowpox which have been obtained from healthy vaccinated animals of the bovine species. The vesicles must be removed and the vaccine must be prepared under aseptic conditions.

The vesicles must be removed from the animal at the time of maximum potency, thoroughly triturated and made into a smooth suspension with an aqueous solution of glycerin. This solution shall not be acid to bromcresol purple T.S. and not distinctly alkaline to phenol red T.S.

Smallpox vaccine is used as a prophylactic before infection with smallpox occurs. A very small quantity of the vaccine is inoculated into the scarified skin and a mild form of the disease results.

The immunity thus acquired is active and is usually of long duration, but it gradually diminishes. Seven years may be taken as the average period of fairly complete protection; then revaccination should be made.

Yellow Fever Vaccine (U. S. P. 1947 to date) consists of a living culture of an attenuated strain of yellow fever virus, selected for high antigenic activity and safety. It is prepared by culturing the virus in the living embryo of the domestic fowl (*Gallus domesticus*). The resulting culture after appropriate processing is distributed in suitable quantities into ampules and dried from the frozen state, after which the ampules are filled with dry nitrogen and hermetically sealed. The vaccine is rehydrated immediately before use. Yellow fever vaccine shall not contain human serum because of a certain icterogenic factor it contains.

Millions of American military personnel have been protected from yellow fever by this vaccine, which is highly satisfactory.

Influenza Virus Vaccine, Types A and B, are made from concentrated virus in allantoic fluid, rendered non-infective by the addition of formaldehyde in 1 to 5000 dilution and given subcutaneously in a single dose of 1 cc.

The vaccine tested in human subjects provided protection to approximately 75 per cent of those vaccinated. The duration of immunity is not fully established, and a repeat dose of 1 cc. at three-month intervals during the influenza season is suggested.

Encephalitis Vaccine, Herpes "F" Strain (Formalin-killed).—Levaditi and Harvier isolated from patients suffering from lethargic encephalitis a strain of herpes virus which was capable of producing encephalitis in rabbits. However, the etiology of the disease is not yet definitely established.

This vaccine is recommended as an aid in the treatment of both the acute and chronic stages of encephalitis.

Encephalitis Vaccine, Japanese Type B, is a formalin-inactivated vaccine prepared from the virus grown on the allantois of the developing chick embryo. A considerable amount of this vaccine was used to immunize members of the United States armed forces.

Equine Encephalomyelitis Vaccine, Eastern Strain and Western Strain, are prepared from formalized chick-embryo cultures and are recommended for the immunization of horses and humans.

Bacterial vaccines or bacterins consist of dead specific bacteria. Suspensions of young, living cultures are killed chemically or by the application of moist heat at a temperature slightly above their thermal death-point. Wright and Douglas first advanced the theory of opsonic action and suggested that the subcutaneous injection of a given species of dead bacteria conferred to the treated individual greater opsonic activity towards the species of organism in question. An opsonin is apparently an antibody in the serum acting upon the invading organisms so as to prepare them for more ready ingestion by the phagocytes. Other antibodies also may have a part in the immunity induced by the injection of these dead organisms.

Bacterial vaccines may be **autogenous,** that is, prepared from a culture of the specific organism isolated from the patient in question; or may be **stock vaccines** prepared from specific organisms that have been cultured in the laboratory for some time.

Some of the more common stock vaccines are the following: Typhoid, Typhoid-Paratyphoid, Cholera, Plague, Acne Combined; Catarrhalis Combined (Respiratory); Coli Combined (VanCott's); Gonococcus; Influenza Combined; Pertussis (Sauer); Pertussis (Special Strength); Pneumococcus Combined; Staphylococcus; Staphylococcus Combined; Streptococcus; Streptoccus Erysipelatus and Bacillus Prodigiosus Toxins (Coley's Mixture); Streptococcus-Staphylococcus; Undulant Fever.

A number of bacterial vaccines also are prepared for veterinary use.

Typhoid Vaccine, Typhoid Bacterial Vaccine, Typhoid Prophylactic, or Enteric Vaccine (U. S. P. 1936 to date) is a sterile suspension in isotonic sodium chloride solution or other suitable diluent of killed typhoid bacilli. The vaccine shall contain in each cubic centimeter at least 1,000 million typhoid organisms.

Typhoid vaccine is used largely as a prophylactic inoculation to actively immunize against typhoid fever. Three doses are given subcutaneously with an interval of about one week between successive doses; the first dose is 0.5 cc., and the following doses each 1 cc.

Typhoid and Paratyphoid Vaccine, Typhoid Combined Vaccine, or Mixed Enteric Vaccine (U. S. P. 1936 to date) is a suspension in isotonic sodium chloride solution or other suitable diluent of killed typhoid bacilli (*Eberthella typhosa*) and killed paratyphoid "A" bacilli (*Salmonella paratyphi*) and killed paratyphoid "B" bacilli (*Salmonella schottmülleri*). The vaccine shall contain, in each cubic centimeter, at least 1,000 million typhoid organisms and at least 250 million each of the paratyphoid organisms.

The uses and the doses are the same as for typhoid vaccine.

Cholera Vaccine, Cholera Bacterial Vaccine, or Cholera Prophylactic Vaccine (U. S. P. 1946 to date) is a sterile suspension in isotonic sodium chloride solution or other suitable diluent, of killed cholera vibrios (*Vibrio comma*) of strains selected for high antigenic efficiency. The vaccine shall contain, in each cubic centimeter, at least 8,000 million cholera organisms.

Two subcutaneous injections of cholera vaccine are given with an interval of seven to ten days between the injections. The first dose is 0.5 cc. and the second dose is 1 cc.

While statistically the results reported on cholera vaccination leave much to be desired, it is considered sufficiently protective to assure enough reduction n morbidity and mortality from cholera to warrant its use.

Plague Vaccine, Plague Bacterial Vaccine, or Plague Prophylactic Vaccine (U. S. P. 1946 to date) is a sterile suspension in isotonic sodium chloride solution or other suitable diluent, of killed plague bacilli (*Pasteurella pestis*) of a strain selected for high antigenic efficiency. Plague vaccine shall contain, in each cubic centimeter, at least 2,000 million plague organisms.

Two subcutaneous doses are given with an interval of ten days between the two doses. The first dose is 0.5 cc. and the second dose is 1 cc.

The results of vaccination against plague have not been easy to evaluate because of the difficulties in obtaining reliable statistics. Probably both the attack rate and the death rate may be reduced by vaccination.

The *Rickettsiæ* form a rather arbitrary group of microörganisms which inhabit the tissues of insects (Arthropods); they live and multiply only within the cytoplasm of living cells.

Exanthematic Typhus Vaccine (U. S. P. 1947 to date) is a sterile suspension of the killed organisms of a strain or strains of epidemic typhus rickettsia (*R. prowazeki*) selected for antigenic efficiency.

The rickettsial organisms are obtained by culturing in the yolk sac membrane of the developing chick embryo (Cox Method). The initial vaccination consists of three injections of 1 cc. each, administered intracutaneously with intervals of from seven to ten days between injections. The prophylactic use of typhus vaccine in typhus-infected countries is believed to be of value in preventing the disease.

Rocky Mountain Spotted Fever Vaccine is a phenol-killed suspension of rickettsia prepared from the tissues of Rocky Mountain wood ticks, or the chick embryo type prepared from the yolk sac, infected with *Rickettsia rickettsii* (*Dermacentroxenus rickettsii*). The protective value is definite but the degree of protection varies with individuals.

Immunogens.—Immunogens are prepared by extracting live organisms with physiological salt solution immediately on removal from the culture medium on which they have grown. Therefore, they consist mainly of products derived from the ectoplasm of the bacterial cells and are specific in their action.

When immunogens are compared by laboratory tests with other antigens, the antibody content of the serum of animals immunized with immunogens always shows the highest antigenic titration.

Immunogens can be used for the same class of cases as bacterial vaccine and clinical results show there are more rapid and intense antigenic effects from them than from bacterial vaccines and they can be safely administered and well tolerated by the patients.

More commonly used immunogens are: Catarrhalis Combined; VanCott's Immunogen Combined; Influenza-Pneumonia Combined; Pertussis; Pneumococcus; Staphylococcus; Streptococcus Combined; Streptococcus (Arthritis).

Bacteriophage.—In 1915 Twort reported a curious degenerative change that he observed during his work with glycerinated calf vaccinia. In 1916–17 d'Herelle published his first work on the lytic principles of filtrates of broth cultures from feces of dysentery patients. d'Herelle named the principle responsible for the lytic action, "Bacteriophage." It is widely accepted that both Twort and d'Herelle described the same phenomenon.

d'Herelle has described the lytic principle as a living, ultra-microscopic organism parasitic upon bacteria, a complete dissolution of the bacterial cell taking place. Studies using the electron microscope have shown some phages to possess rounded and others cubical forms. Some of these organisms apparently have a flagellum. Bacteriophage can be propagated through an unlimited series of bacterial cultures provided they are young, actively multiplying and susceptible. The phenomenon of bacteriophage is twofold—a dissolution of the bacterial cell takes place and in the course of this the bacteriophage principle reproduces itself.

Bacteriophage may be isolated from several different sources. It has been shown to be present in the intestinal contents of normal man and animals, in the blood, urine and pus of those who are convalescents from bacterial infections, and in sewage water. It is also occasionally found in old laboratory cultures.

Bacteriophage is not, as a rule, strictly specific for a given species but is usually more active against one species, less active against closely related species and still less active against unrelated species. It has been shown by Burnet that phage specificity is associated with the antigenic structure of the bacteria.

Bacteriophage as such cannot be isolated in a pure form. It will pass through porcelain filters and ultrafilters, thus it can be obtained in the broth filtrate, free of bacteria.

Since bacteriophage brings about complete dissolution of susceptible bacteria in the test-tube, d'Herelle believes that bacteriophagy is directly involved in recovery from infectious diseases. A review of the clinical reports of bacteriophage therapy indicates that it is very useful in staphylococcus, streptococcus and non-specific urinary infections and to a certain extent in enteric infections.

The principal commercial forms are as follows: Staph-bacteriophage, Strept-bacteriophage, Coli bacteriophage, Staph-coli bacteriophage.

TUBERCULINS

Tuberculins are preparations made in a number of ways from the human and bovine strains of the tubercle bacillus and are used both in diagnosis and treatment. The active substance of the tuberculin, which is apparently an albuminous derivative insoluble in alcohol, is elaborated by the organisms during their multiplication. In human, as well as in veterinary practice, tuberculin may be applied as a diagnostic agent to determine whether the person or animal is or has been infected with mycobacterium. The tuberculin may be applied by intracutaneous injection, by rubbing into the scarified skin, by dropping into the eye, or by other methods. In each case a marked redness or inflammation indicates a positive reaction.

Tuberculin must be capable of effecting a general and local response in tuberculous guinea-pigs.

Tuberculin is used mostly as a diagnostic agent, but also sometimes as a curative agent. Average dose, by intracutaneous injection, 0.001 cc.

TOXINS, TOXOIDS AND VENINS

Toxins are antigens that have the power of stimulating certain cells of the animal body to produce antitoxins.

Endotoxins are present in the bacterial vaccines (page 66) and refer to toxins which do not diffuse out of the intact bacterial cells.

Endotoxins are soluble toxins and diffuse out of the intact bacterial cells. To produce commerciel exotoxins, the highly virulent organisms are cultured in bouillon and killed with an antiseptic; the product is then filtered to produce the dead organisms and standardized upon a suitable animal for the minimum lethal dose. As commercial toxins are essential for the production of antitoxins, at least as many are produced as there are antitoxins (see pages 74 to 76).

Some plants also produce toxlns (ricin, abrin, etc.), though these are of the endotoxic type.

Old Tuberculin, Tuberculin-Koch, Concentrated Tuberculin, Crude Tuberculin (U. S. P. 1936 to date) is a sterile solution in a special liquid culture medium of the soluble products of growth of the tubercle bacillus (*Mycobacterium tuberculosis*), and should contain about 50 per cent of glycerin.

Purified Protein Derivative of Tuberculin (U. S. P. 1947 to date) is a sterile soluble product of the growth of the tubercle bacillus (*Mycobacterium tuberculosis*) prepared in a special liquid medium free from protein.

As an agent for the diagnosis of tuberculosis it has the distinct advantage of being a practically pure specific tubercle protein, and free from residual constituents of the synthetic medium in which the product is developed.

To produce commercial **Exotoxins**, the highly virulent organisms are cultured in bouillon and killed with an antiseptic; the product is then filtered to remove the dead organisms and standardized upon a suitable animal for the minimum lethal dose. This dose is the smallest amount of the toxin that will cause the death of a guinea-pig (weighing between 250 and 280 gm.) within ninety-six hours after subcutaneous administration. As commercial toxins are essential for the production of antitoxins, at least as many are produced as there are antitoxins (see pages 74 to 76).

Toxoids are modified toxins in which the toxic powers are greatly reduced, but the ability to induce active immunity remains.

Venins are similar to exotoxins, but are produced by animals (snakes, toads, scorpions, etc.).

Snake Venins are obtained by irritating poisonous snakes, held facing a sheet of paper tied over a conical glass container. The snake "strikes" the paper, which is penetrated by its fangs, and the semi-liquid "poison" is ejected into the glass container or retained on the inner side of the paper. Mixtures of venins from the poisonous snakes of a locality, country or continent are prepared and used for the preparation of polyvalent antivenins.

The **Fer-de-Lance Venom Solution** is used as a hemostatic for local application to bleeding areas. The **Moccasin Venom** in 1 to 3000 saline solution is used hypodermically for the control of certain hemorrhagic conditions.

Poisonous snakes of North America include rattlesnakes, coral snakes, copperheads and water moccasins; those of Central and South America include the bushmaster, Fer-de-lance, tropical rattlers and palm vipers; those of Africa include the boomslang, cobras, mambas, puff adder and gaboon viper; those of India include the cobras, kraits and sea snakes of the Indian Ocean.

Diagnostic Diphtheria Toxin, Schick Test Toxin (U. S. P. 1936 to date) is a sterile solution of the toxic products of growth of the diphtheria bacillus (*Corynebacterium diphtheriæ*).

This toxin is used to determine the antitoxic power of the patient. If the patient possesses a fair degree of immunity against diphtherial infection, the toxin used will cause no irritation or redness, for its toxic powers have been overcome by the antitoxin present in the serum or plasma of the patient. If irritation or redness occurs, the patient is not immune to diphtherial infection. Average intracutaneous dose for determining susceptibility, 0.1 cc. of the dilution, representing one-fiftieth of the minimum lethal dose.

Scarlet Fever Streptococcus Toxin, Dick Test Toxin (U. S. P. 1936 to date) is a sterile solution in a medium containing not more than 1 per cent of peptone but no meat extractives, of certain products, including a soluble toxin, resulting from the growth in the broth of suitable strains of hemolytic streptococci (*Streptococcus scarlatinæ*).

The potency of the toxin shall be expressed in terms of the skin test dose, which is the smallest quantity of toxin, injected intracutaneously, that will give positive reactions in any person susceptible to scarlet fever, and negative reactions in any person immune to scarlet fever.

Average intracutaneous dose for determining sus eptibility (Dick Test) is 0.1 cc. of the dilution, representing one skin test dose; for prophylactic use graded hypodermic doses are given at proper intervals until a negative Dick Test is obtained.

Diphtheria Toxoid, Diphtheria Anatoxin or Anatoxin-Ramon (U. S. P. 1936 to date) is a sterile aqueous solution of the products of growth of the diphtheria bacillus (*Corynebacterium diphtheriæ*) so modified by special treatment as to have lost the ability to cause toxic effects in guinea-pigs but retaining the property of inducing active immunity. The toxicity of diphtheria toxoid shall be so low that five times the dose for the adult human does not cause either local or general symptoms of diphtheria poisoning in a guinea-pig within thirty days after its injection into the animal. The antigenic value shall be such that the initial dose for humans shall protect at least 80 per cent of guinea-pigs, six weeks after injection, against five minimum lethal doses each of diphtheria test toxin.

Diphtheria toxoid, when administered subcutaneously, acts as an antigen, stimulating certain cells of the patient to produce antitoxin, thus immunizing against diphtherial infection. Average dose. hypodermic, for active immunization, 1 cc. or 0.5 cc. (as may be specified on the label), to be repeated twice at intervals of approximately three weeks between injections.

Alum-precipitated Diphtheria Toxoid (U. S. P. 1942 to date) is a sterile suspension of diphtheria toxoid precipitated with alum from the solution in which the products of growth of the diphtheria bacillus (*Corynebacterium diphtheriæ*) have developed and have been so modified by special treatment as to have lost the ability to cause toxic effects in guinea-pigs, but retaining the property of inducing active immunity.

After injection, alum-precipitated toxoid is slowly absorbed, thus acting as a continuous and progressive stimulant to the defensive mechanism of the body. This preparation is well tolerated by young children, but in older patients reactions may occur. Two doses are generally given of 0.5 cc. or 1 cc. each with an interval of one week.

Tetanus Toxoid (U. S. P. 1942 to date) is a sterile solution of the products of growth of the tetanus bacillus (*Clostridium tetani*), so modified by special treatment as to have lost the ability to cause toxic effects in guinea-pigs, but retaining the property of inducing active immunity.

Average prophylactic dose: 0.5 cc. or 1 cc. to be repeated at an interval of approximately three weeks.

Alum-precipitated Tetanus Toxoid, Refined Tetanus Toxoid (U. S. P. 1942 to date) is a sterile suspension of tetanus toxoid, precipitated with alum from a solution in which the products of growth of the tetanus bacillus (*Clostridium tetani*) have developed and have been so modified by special treatment as to have lost the ability to cause toxic effects in guinea-pigs but retaining the property of inducing active immunity.

Average dose: hypodermic for active immunization, 1 cc. (or 0.5 cc.), to be repeated once with an interval of four to six weeks.

ANTITOXINS AND ANTIVENINS

Antitoxins or Antitoxic Serums are prepared from the blood of horses which have been immunized by repeated injections of specific bacterial toxins. The toxin, in constantly increasing doses, induces the formation of antitoxin in great excess which appears in the blood serum of the injected animal. The animal is bled, the clot permitted to form and the clear supernatant serum separated for use, or the globulins bearing the antitoxic substance are "salted out." Antitoxins in the dried globulins can be preserved indefinitely.

The following commercial antitoxins are produced: Diphtheria, Tetanus, Gas Gangrene (Perfringens), Botulinus, Scarlet Fever.

Antivenins are prepared in the same manner as antitoxins and possess the same general characteristics. North American, South American and African polyvalent antivenins and several univalent forms are commercially produced.

Diphtheria Antitoxin, Purified Antidiphtheric Serum, or Antidiphtheric Globulins (U. S. P. 1905 to date) is a sterile solution of antitoxic substances obtained from the blood serum or plasma of a healthy animal which has been immunized against diphtheria toxin.

After the serum or plasma from the immunized animal has been collected, the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in freshly distilled water. Sodium chloride and a preservative are then added and the solution is filtered through a bacteria-excluding filter. Diphtheria antitoxin has a potency of not less than 500 antitoxic units per cubic centimeter.

The antitoxic unit is the amount of diphtheria antitoxin necessary to prevent the death of a guinea-pig, weighing between 250 and 280 gm. when injected with 100 minimum lethal doses of the same lot of toxin used to stimulate the production of the antitoxin. Average therapeutic dose by parenteral injection, 20,000 units; prophylactic dose, 1,000 units.

Antitoxins and antivenins give a valuable passive immunity when injected before infection has taken place. They are valuable curative agents also, when used in sufficient amount to neutralize the pathogenic effects of the toxin developed in the patient. This is especially true when these agents are used early in the disease and before the pathogenic effects are too far advanced.

Diphtheria Antitoxin of U. S. P. 1905 to 1916 was defined as a fluid separated from the coagulated blood of a horse, immunized through the inoculation of diphtheria toxin. The therapeutic dose was 3,000 units and the prophylactic dose 500 units. This preparation has been deleted and is no longer used. Sensitization of patients to horse-serum proteins, which frequently occurred, gave rise to serious complications.

Dried Diphtheria Antitoxin of U. S. P. 1916 to 1926 was obtained by the evaporation of diphtheria antitoxin or purified diphtheria antitoxin in a vacuum over sulfuric acid or other desiccating agent or by passing over it a current of warm air freed from bacteria. The average therapeutic dose was 10,000 units and the prophylactic dose 1,000 units. This preparation was deleted from the Pharmacopœia largely because of the difficulty experienced by physicians in preparing suitable solutions of the dried serum without contamination with air-borne bacteria.

Scarlet Fever Streptococcus Antitoxin, Scarlet Fever Antitoxin or Anti-Scarlet Fever Globulins (U. S. P. 1936 to date) is a sterile solution of antitoxic substances obtained from the blood serum or plasma of a healthy animal which has been immunized against the toxin produced by the streptococcus regarded as causative of scarlet fever. The potency of this antitoxin is not less than 400 antitoxic units per cubic centimeter. Average therapeutic dose by parenteral injection, 6,000 units; prophylactic dose, 2,000 units. The diagnostic dose for aid in determining the nature of a rash (Schultz-Charlton Test), intracutaneous into erythematous eruptions, is not to exceed 0.2 cc.

Tetanus Antitoxin, Purified Antitetanic Serum, Antitetanic Globulins (U. S. P. 1916 to date) is a sterile solution of antitoxic substances obtained from the blood serum or plasma of a healthy animal which has been immunized against tetanus toxin. It has a potency of not less than 400 antitoxic units per cubic centimeter. The method of preparation is the same as for diphtheria antitoxin Average therapeutic dose by parenteral injection is 20,000 units; prophylactic dose is 1,500 units.

Tetanus Antitoxin (U. S. P. 1916 to 1926) was a fluid, having a potency of not less than 100 units per cubic centimeter, separated from the coagulated blood of the horse or other large domestic animal, which has been properly immunized against tetanus toxin. The average therapeutic dose was 10,000 units and the prophylactic dose 1,500 units. This preparation is no longer used because of the possibility of sensitization of the patient to horse serum.

Dried Tetanus Antitoxin (U. S. P. 1916 to 1926), prepared in the same manner as Dried Diphtheria Antitoxin, has been discontinued in medical practice because of the danger of bacterial contamination in the preparation for injection.

Tetanus and Gas Gangrene Antitoxin (U. S. P. 1947 to date) is a sterile solution of antitoxic substances obtained from the blood of healthy animals immunized against the toxins of *Clostridium tetani* and *C. perfringens* and *C. septicum.* Each package contains not less than 1,500 units of tetanus antitoxin and not less than 2,000 units of each of the other component antitoxins. The average parenteral dose as a prophylactic is the contents of one or more packages.

Bivalent Gas Gangrene Antitoxin (U. S. P. 1947 to date) is a sterile solution of antitoxic substances obtained from the blood of healthy animals, which have been immunized against *Clostridium perfringens* and *Clostridium septicum* toxins. Each package of bivalent gas gangrene antitoxin shall contain not less than 10,000 antitoxic units of each of the component antitoxins.

Trivalent Gas Gangrene Antitoxin (U. S. P. 1947 to date) is a sterile solution of antitoxic substances obtained from the blood of healthy animals which have been immunized against the toxins of *Clostridium perfringens, Clostridium septicum* and *Clostridium œdematiens* (Novyi). Each package of trivalent gas gangrene antitoxin shall contain not less than 10,000 units of *Clostridium perfringens* and *Clostridium septicum* antitoxins, and 1,500 units of *Clostridium œdematiens* (Novyi) antitoxin.

Pentavalent Gas Gangrene Antitoxin (U. S. P. 1947 to date) is a sterile solution of antitoxic substances obtained from the blood of healthy animals which have been immunized against the toxins of *Clostridium perfringens, Clostridium septicum, Clostridium œdematiens* (Novyi), *Clostridium bifermentans* (Sordelli), and *Clostridium histolyticum.* Each package of pentavalent gas gangrene antitoxin shall contain not less than 10,000 units each of *Clostridium perfringens* and *Clostridium septicum* antitoxins, 3,000 units of *Clostridium histolyticum* antitoxin, and 1,500 units each of *Clostridium œdematiens* (Novyi) and *Clostridium bifermentans* (Sordelli) antitoxins.

The several admixtures of gas gangrene antitoxins are designed for use in varying degrees of gas gangrene infection. The average dose, parenteral, therapeutic, or prophylactic, of any of these mixtures is the contents of one or more packages as the initial dose.

Antivenins have been prepared for use in many parts of the world. **North American Anti-Snake-Bite Serum** is a purified and concentrated serum globulin obtained from the blood of horses which have been immunized with snake venoms of North American snakes. This preparation will act as an antidote for the poisons of the copperhead, cotton mouth moccasin and the rattlesnakes.

Tropical American Anti-Snake-Bite Serum (Bothrops antivenin) is prepared from and effective against venoms of the principal poisonous snakes of the genus *Bothrops,* especially *B. atrox* (the Fer-de-lance).

Antivenin Cascabel or **Tropical Rattler Anti-Snake-Bite Serum** is prepared from and effective against the venom of the tropical rattler.

ANTIBACTERIAL SERUMS

Antibacterial serums correspond to antitoxins and antivenins, except that their production in animals is stimulated by endotoxins rather than exotoxins. Therefore injections of the bacterial cells, as found in vaccines or bacterial vaccines, are required. The destruction of the injected cells by the phagocytes tends to liberate in the blood stream several antigens which stimulate the production of several corresponding antibodies. The antibody complex in antibacterial serums is not very well known.

The prophylactic and curative effects of antibacterial serums are not as pronounced and definite as in the case of antitoxins and antivenins.

Some of the better known commercial antibacterial serums are the following: Anti-anthrax, Antidysenteric, Antimeningococcic, Antipneumococcic, Antistreptococcic, Antiplague (Yersin's Serum) and many polyvalent serums.

Antimeningococcic Serum, Meningitis Serum (U. S. P. 1936 to 1947; N. F. 1947 to date) is obtained from the blood of an animal immunized with cultures of the several types of meningococci (*Neisseria intracellularis*) which prevail in the United States. Average therapeutic dose by parenteral injection, 20 cc.

Antipneumococcic Serum, Pneumonia Serum—Type Specific (U. S. P. 1936 to 1947; N. F. 1947 to date) is obtained from the blood of an animal which has been immunized with cultures of a pneumococcus (*Diplococcus pneumoniæ*) of one of the types for which a serum has been prepared. Average therapeutic dose by parenteral injection, 20,000 to 100,000 units.

HUMAN SERUMS AND GLOBULINS

Human Serums and **Globulins** containing antibodies are useful in treating certain diseases for which they are recommended.

Human Immune Globulin, Measles Prophylactic or Placental Extract (U. S. P. 1942 to date) is a sterile solution of antibodies obtained from the placental blood and the placentæ expelled by healthy women.

This serum is efficacious in preventing or modifying the attack of measles in exposed, susceptible subjects. The preventive dose ranges from 2 cc. to 4 cc. The dose for modifying the disease after its development is from 3 cc. to 10 cc. depending on the stage of the attack at the time of administration.

Human Measles Immune Serum, Measles Convalescent Serum (U. S. P. 1942 to 1947; N. F. 1947 to date) is sterile serum obtained from the blood of a healthy human who has survived an attack of measles. This serum is efficacious in preventing or modifying an attack of measles in susceptible persons who have been exposed. The average doses are: therapeutic, 20 cc.; prophylactic, 10 cc.

***Human Scarlet Fever Immune Serum, Scarlet Fever Convalescent* Serum** (U. S. P. 1942 to 1947; N. F. 1947 to date) is a sterile serum obtained from the blood of a healthy human who has survived an attack of scarlet fever. The average doses are: therapeutic, 20 cc.; prophylactic, 10 cc.

Lactic Acid Organisms.—Metchnikoff advanced the theory that duration of life might be prolonged if measures were taken to control intestinal putrefaction. He found that there was a widespread popular belief in the advantage of a diet consisting largely of sour milk, and that there was a fair parallel between unusual longevity and such a diet. He also observed that the cause of much sickness and debility was due to gastro-intestinal auto-intoxication. Lactic acid, due to the action of *Lactobacillus lactisacidi,* in the beverages known as koumys, kefir, yoghurt, rapi and buttermilk, tends to inhibit intestinal putrefaction. This and other organisms (*Lactobacillus bulgaricus* and *L. acidophilus*), especially active in lactic acid production, are prepared in the form of tablets or in suspension in liquids. When such preparations are taken into the stomach, the organisms are not all killed, but pass into the intestines where the bacterial reproduction and lactic acid formation are very active. When these preparations are added to sterile milk, souring ensues and enormous numbers of the bacilli are produced. "Kefir fungi" is a mixture of bacteria and yeast sold in dry form and capable of producing lactic acid fermentation in milk.

Nitrogen-fixing Bacteria.—Nodules or tubercules on the roots of leguminous plants (clovers, alfalfa, soy bean, etc.) contain bacteria (*Pseudomonus radicicola*) which have the power of converting atmospheric nitrogen into nitrogenous compounds soluble in the sap of the plant, thus providing for a marked increase in growth of the plant. The bacteria live upon the food materials in the sap of the plant and thus a true symbiosis results. Pure cultures of the organism can be successfully inoculated into the roots of leguminous plants, and by scattering dried cultures of these nitrogen-fixing bacteria in the soil, infection of the growing plants usually results. The production and use of such inoculants is an important phase of agriculture.

Applied Bacteriology.—In the brief space allotted in a few pages, it is impossible to cover adequately even the more important phases of applied bacteriology. Mention cannot be made of many products which are based upon the presence of bacteria or which are due to bacterial action, neither can a detailed discussion be given relative to many industrial operations which depend upon bacterial activity, such as the curing of vanilla, the fermentation of tobacco, the manufacture of vinegar, the tanning of hides, the ripening of cheese and the retting of flax.

Bacteriology as an applied science consists of several special branches, the most important of which are Pathological Bacteriology, Public Health Bacteriology, Dairy Bacteriology, Soil Bacteriology, and Household Bacteriology.

ANTIBIOTIC AGENTS

Antibiotics, from antibiosis meaning "antagonistic association between organisms to the detriment of one of them," have become very important therapeutic agents within recent years.

Penicillin

Penicillin was first found by Fleming in 1929. Later, in 1940, a group of Oxford chemists demonstrated its possibilities in medicine.

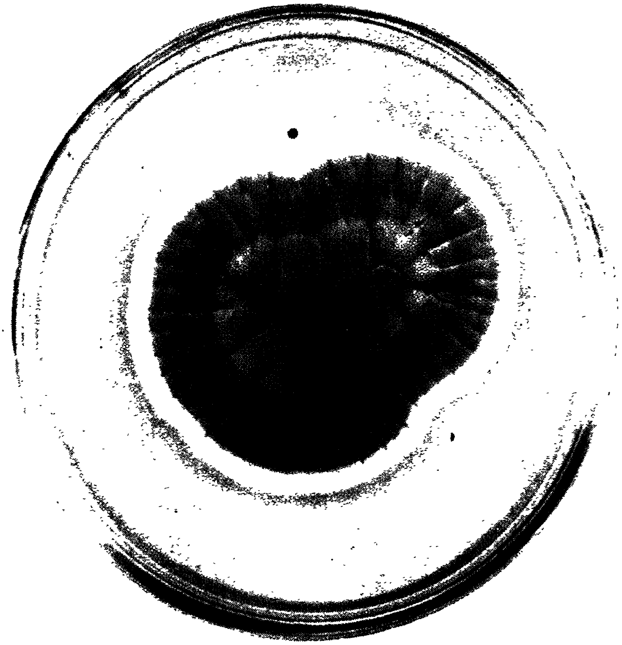
PREPARATION.—Penicillin is found in cultures of *Penicillium notatum* and of P. chrysogenum. Definite strains of the mold are used and may be grown using either the surface or submerged culture method. Commercially it is extracted from these cultures by means of organic solvents such as ether, amyl acetate, chloroform and others.

USES AND DOSE.—Penicillin is most active on Gram-positive bacteria but the Gram-negative *Neisseria* species are notable exceptions. Largely due to the experience with the wounded and sick in the armed forces (1942 to 1946), it has been established that penicillin may be used successfully in the treatment of a wide variety of diseases, such as those caused by streptococci, staphylococci, gonococci, the bacilli of gas gangrene, and of anthrax, and actinomyces. Encouraging results are being obtained in the treatment of syphilis and also Weil's disease.

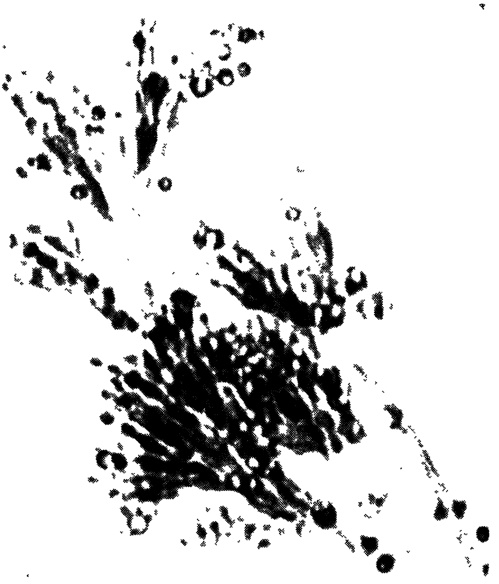
Clinically there have been no serious toxic effects and inasmuch as penicillin contains variable amounts of impurities it is altogether possible those effects that are observed may be due to this fact. Chills, fever and urticarial conditions are the most common untoward effects.

Penicillin is usually combined with calcium or sodium for therapeutic use. These preparations are more stable and somewhat more slowly absorbed and therefore exert their effects over a longer period of time. Penicillin may be administered intramuscularly, intravenously, intrathecally, topically and orally. Penicillin in oil suspension may be

PLATE II

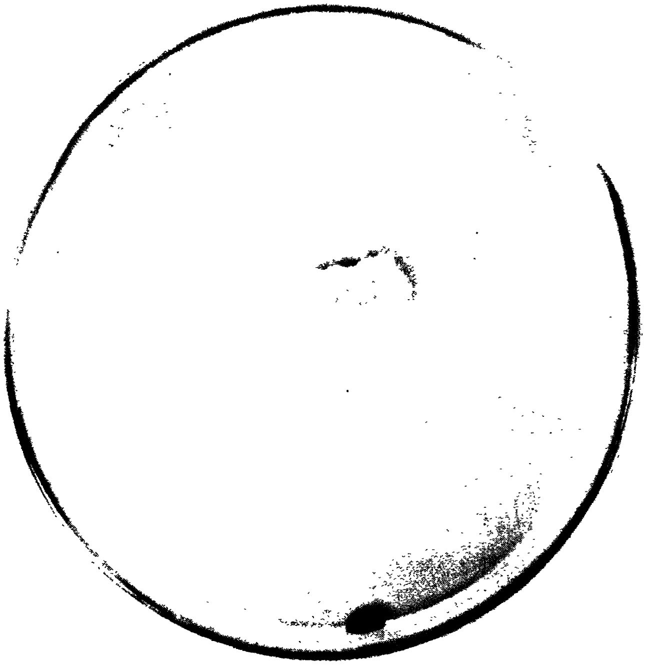


Penicillium notatum N.R.R.L. 1249.B21, descendant of Fleming's strain, used in nearly all surface culture production of penicillin. (Courtesy of Eli Lilly and Company.)



Penicillium notatum showing the penicillus, or spore-bearing head, which identifies a *Penicillium*. (990X.) (Courtesy of Eli Lilly and Company.)

PLATE III



Streptomyces griseus which forms streptomycin when grown by surface culture technique or in submerged culture in fermentation tanks (Courtesy of Eli Lilly and Company.)

Actinomyces griseus, producer of streptomycin. (3430X.) (Courtesy of Eli Lilly and Company.)

injected in very large doses: 300,000 units, intramuscularly, and the effect will extend over two or three days.

Commercial penicillin is not a pure substance but a mixture of several fractions. At the present time, four of these are known and are designated in the United States as G, X, F and K. The relative amounts of these four fractions may vary in commercial penicillins. These fractions differ in their *in vitro* and *in vivo* activity against a variety of bacteria. This condition leads to variable results in therapy. Manu*facturers coöperating with the National Institute of Health* are *trying to improve the preparation of penicillin and produce a more uniform* product.

STANDARDS.—Penicillin is standardized in terms of its antibacterial activity and for this purpose a unit of value *originally* used by the Oxford workers is now known as the Oxford or Florey unit. A unit is equivalent to the smallest amount, which when dissolved in 50 cc. of meat extract broth, completely inhibits the growth of the test strain of *Staphylococcus aureus.*

Pure crystalline sodium penicillin G having 1666 units per mg. has been designated as the international standard. The new international unit has been defined as "the specific penicillin activity contained in 0.6 microgram of the international standard."

The following penicillin items are recognized in the U. S. P.

Penicillium Calcium (U. S. P. 1947 to date).
Penicillium Sodium (U. S. P. 1947 to date).
Penicillium Dental Cones (U. S. P. 1947 to date).
Penicillin Injection in Oil and Wax (U. S. P. 1947 to date).
Penicillin Ointment (U. S. P. 1947 to date).
Penicillin Tablets (U. S. P. 1947 to date).
Penicillin Troches (U. S. P. 1947 to date).

Streptomycin

More recently Waksman, Bugie and Schatz (1944) isolated an antibiotic agent from *Streptomyces griseus* (*Actinomyces griseus*) and named it "Streptomycin." The organism is grown in a suitable medium using the submerged culture type of fermentation. When maximum growth is reached, the broth is separated from the organism and the active agent extracted from it by absorption on carbon, subsequent elution and precipitation.

This agent shows remarkable activity against Gram-negative bacteria including the rod forms but also affects Gram-positive organisms. *In vitro* studies indicate a strong bacteriostatic action against *Mycobacterium tuberculosis.* Its chief value, to date, is that it is active against pathogens not affected by penicillin.

Its use as a therapeutic agent is still in the experimental stage and the results are far from decisive. It has shown remarkable efficiency in treating those ill of tularemia cases clearing up in a few days. It is also of value in treating urinary infections caused by Gram-negative organisms. Its effect in treating cases of pulmonary tuberculosis, typhoid and brucellosis shows some promise.

It has a low toxicity and may be administered in large doses, but undesirable reactions such as chills, fever, pains in the joints and a histamine-like lowering of the blood pressure have been observed. However, streptomycin appears to be a promising antiobic substance which will rank with penicillin as a valuable therapeutic agent.

Tyrothricin

Another well known antibiotic is Tyrothricin, which is a mixture of gramicidin and tyrocidine produced by *Bacillus brevis*, and was discovered by Dubos in 1939. Its toxicity and lack of solubility limits its use to local therapy against certain of the Gram-positive pathogenic microörganisms. It has proved to be a successful therapeutic agent in treating infected wounds, sinusitis, etc.

ALGÆ

BACILLARIACEÆ, OR DIATOMS

PURIFIED SILICEOUS EARTH

Siliceous Earth consists of the frustules, whole or broken, of diatoms, and occurs in natural deposits. The material is mined, usually calcined to destroy the organic matter, then washed and dried.

Purified Siliceous Earth, Purified Kieselguhr or Purified Infusorial Earth (U. S. P. 1916 to date) is a form of silica consisting of the frustules and fragments of diatoms, purified by boiling with diluted hydrochloric acid, washing and calcining.

Description.—A very fine but gritty, white, light gray or pale buff, odorless powder, insoluble in water, but readily absorbing about four times its weight of water. For **Tests of Identity and Purity** see the U. S. Pharmacopœia.

Microscopic Examination.—In Purified Siliceous Earth, the living portion of the diatom is entirely removed, leaving only the siliceous coat or shell; however, the diatoms are identified by the microscopic markings on these frustules.

To prepare a mount, place a small quantity of the material, in a small vial, nearly fill it with distilled water, shake vigorously, at once transfer a small quantity of the mixture to another vial containing water, shake well and transfer 10 minims to a clean slide; view in the water or allow the water to evaporate, pass the slide through a flame and mount in Canada balsam.

In the identification of the various genera and species, it is necessary to bear in mind that there are two and sometimes three views presented in the mount of the same species of diatom. Some of the common forms of diatoms occurring in commercial siliceous earth are shown in Figure 13.

PHÆOPHYCEÆ, OR BROWN ALGÆ

The **Algæ** of present economic importance are mostly marine forms, collectively known as seaweeds, and belong to the brown algæ (*Phæophyceæ*) and the red algæ (*Rhodophyceæ*). The marine Algæ, as a whole, grow most abundantly, and probably constitute a greater mass of vegetative matter than that of all of the land plants. Because of their carbohydrate mucilage content, seaweeds are used to some extent as human and stock food and for manures. They also yield **iodine** (U. S. P. 1831 to date) in their ash, 0.02 to 0.20 per cent of the dry plant.

Laminaria consists of the cylindrical stipes and basal portions of the midribs of the fronds of *Laminaria digitata* and *L. cloustonii* (Fam. *Laminariaceæ*). The former is a very characteristic kelp which is common north of Cape Cod. The fronds are attached to the rocks and the stout and solid stipe is from 3 to 15 dm. in length, more or less cylindrical below, compressed above and free from distinct mucilaginous cavities (muciparous glands).

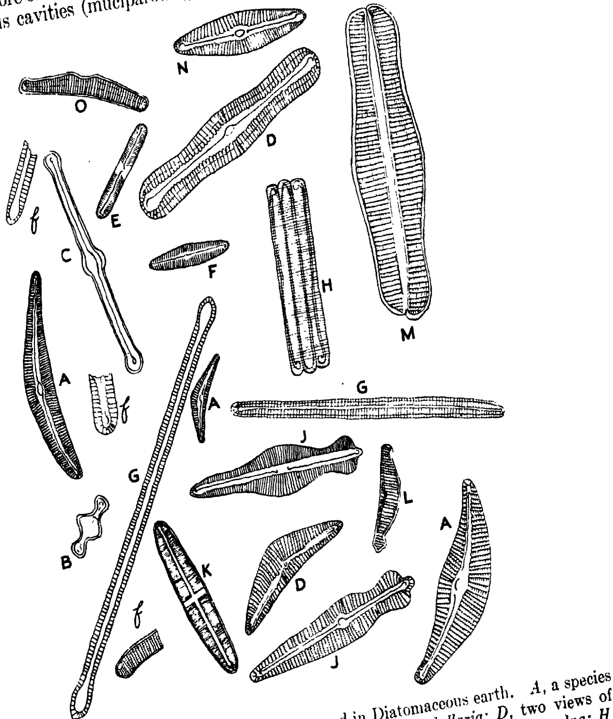


FIG. 25.—Some common forms of diatoms found in Diatomaceous earth. *A*, a species of *Cymbella*; *B*, *Tabellaria floccolsa*; *C*, another species of *Tabellaria*; *D*, two views of *Navicula viridis*; *E*, *Navicula phoenecenteron*; *F*, *Navicula lacustris*; *G*. *Synedra ulna*; *H*. several frustules of a *Navicula*; *J*, *Gomphonema geminatum*; *K*, a species of *Stauroneis*; *L*, *Epithemia hyndmannii*; *M*, some frustules of *Epithemia*; *N*, *Pinnularia brebessonii*; *O*. *Eunotia diodon*; *f*, fragments of broken diatoms. (Identified by Charles Boyer, drawn by W. F. Haase.)

L. cloustonii is a common European form and resembles *L. digitata*. The pieces as dried for commerce are tough, horny, and grayish to dark brown in color. The drug contains about 47 per cent of mucilage, and iodine from 0.06 to 0.11 per cent.

The dry material increases six-fold upon the absorption of water, hence it has been used to absorb moisture from the parts to which it is applied and to enlarge openings through the gentle swelling of the mucilage. As it cannot be sterilized without losing these properties, it has been largely replaced by other materials.

Fucus or **Bladderwrack** (N. F. 1916 to 1926) is the dried thallus of *Fucus vesiculosus, Fucus serratus, Fucus nodosus* or *Fucus siliquosus* (Fam. *Fucaceæ*). The plants are common seaweeds growing on rocks near the coast of the northern countries bordering the Atlantic Ocean. The fruiting plants are most active medicinally and are collected in autumn, although fructification continues during the winter, or may be seen to some extent at any time during the year. A number of other species of *Fucus*, as well as other *Algæ*, are gathered under the name of **kelp** off the coast of Cherbourg, France, and Glasgow, Scotland, and are used as a source of iodine and bromine.

The drug is blackish brown, cartilaginous, with a seaweed-like odor and a mucilaginous, somewhat saline and nauseous taste.

Fucus contains from 22 to 62 per cent of carbohydrate substances, consisting mostly of mucilage (algin) and a peculiar cellulose; and from 3 to 24 per cent of total ash, containing from 0.7 to 1 per cent of iodine and some bromine.

The drug should contain not more than 3 per cent of foreign organic matter and yield not more than 4 per cent of acid-insoluble ash.

Fucus has been used as an alterative and in the treatment of obesity. Average dose, 0.6 gm.

Sodium Alginate or Algin (N. F. 1947 to date) is the purified carbohydrate product extracted from giant brown seaweeds by the use of dilute alkali. It consists chiefly of the sodium salt of alginic acid, a polyuronic acid composed of beta-mannuronic acid residues, linked so that the carboxyl group of each unit is free while the aldehyde group is shielded by a glycosidic linkage.

Sodium Alginate occurs as a nearly odorless and tasteless, coarse or fine powder, yellowish-white in color. It is readily soluble in water, forming a viscous, colloidal solution. It is insoluble in alcohol, ether, chloroform and in strong acid.

For tests of identity and purity see the National Formulary.

Sodium Alginate is used in the food industry (ice cream, water ices, chocolate milk, salad dressings, icings, confectionery), and as a mucilage for suspending pharmaceutical and cosmetic mixtures; also as a sizing and for other industrial purposes.

Aluminum Alginate, formed from algin and aluminum metal, is used for stomach ulcers, and to carry penicillin through the stomach to the intestines where it is absorbable.

RHODOPHYCEÆ, OR RED ALGÆ

Agar

Agar, Chinese, Japanese or Californian Agar (U. S. P. 1916 to date) is the dried, mucilaginous substance extracted from *Gelidium cartilagineum* (Linné) Gaillon (Fam. *Gelidiaceæ*) and from related red *Algæ*.

These algæ grow along the eastern coast of Asia and the western coast of North America.

Agar is prepared in California as follows: The fresh seaweed is washed for twenty-four hours in fresh running water; extracted in steam-heated digesters with dilute agar solution and then with water for a total period of about thirty hours. The hot aqueous extract is cooled and then congealed in ice machines. The water from the agar almost completely separates as ice. The 300-pound agar ice block (containing about 5 pounds of dry agar) is crushed, melted and filtered through a rotary vaccum filter. The moist agar flakes are then dried by currents of dry air in tall cylinders. The fully dried product can be reduced to a fine powder.

Description and Histology.—See U. S. Pharmacopœia and Figure 26.

Constituents.—Agar is a long-chain polysaccharide, the repeating unit of which contains nine *d*-galactose residues terminated by one *l*-galactose residue, each *l*-galactose residue being esterified with sulfuric acid. Agar also contains about 6 per cent of a nitrogen-containing substance and 3.5 per cent of cellulose.

Standards.—Agar contains not more than 1 per cent of foreign organic matter, yields not more than 1 per cent of acid-insoluble ash and not more than 20 per cent of moisture.

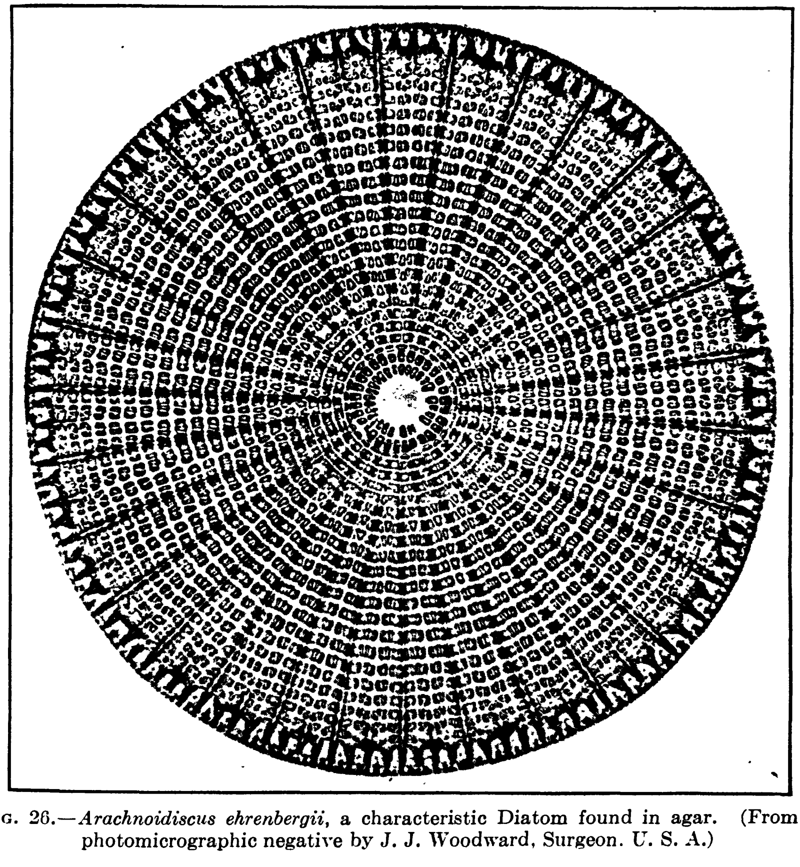


Fig. 26.—*Arachnoidiscus ehrenbergii*, a characteristic Diatom found in agar. (From a photomicrographic negative by J. J. Woodward, Surgeon. U. S. A.)

Agar is insoluble in cold water, but if 1 part of agar be boiled for about ten minutes with 100 parts of water, it yields a stiff jelly upon cooling. An aqueous solution of agar, 1 in 100, cooled to 50° C., shows no turbidity within ten minutes, when mixed with an equal volume of picric acid T.S. (absence of gelatin), or gives more than a slightly reddish or reddish violet color upon the addition of iodine T.S.

Uses and Dose.—Agar is used in medicine as an emollient laxative. Average dose, 10 gm. Agar is extensively used as a gel in bacteriological culture media and in industry for making emulsions; for thickening milk, cream and ice cream; in adhesives; and for sizing textiles, especially silks.

CHONDRUS

Chondrus, Irish Moss or Carrageen (U. S. P. 1842 to 1926; N. F. 1926 to date) is the dried bleached plant of *Chondrus crispus* (Linné) Stackhouse or of *Gigartina mamillosa* (Goodenough et Woodward) J. Agardh (Fam. *Gigartinaceæ*).

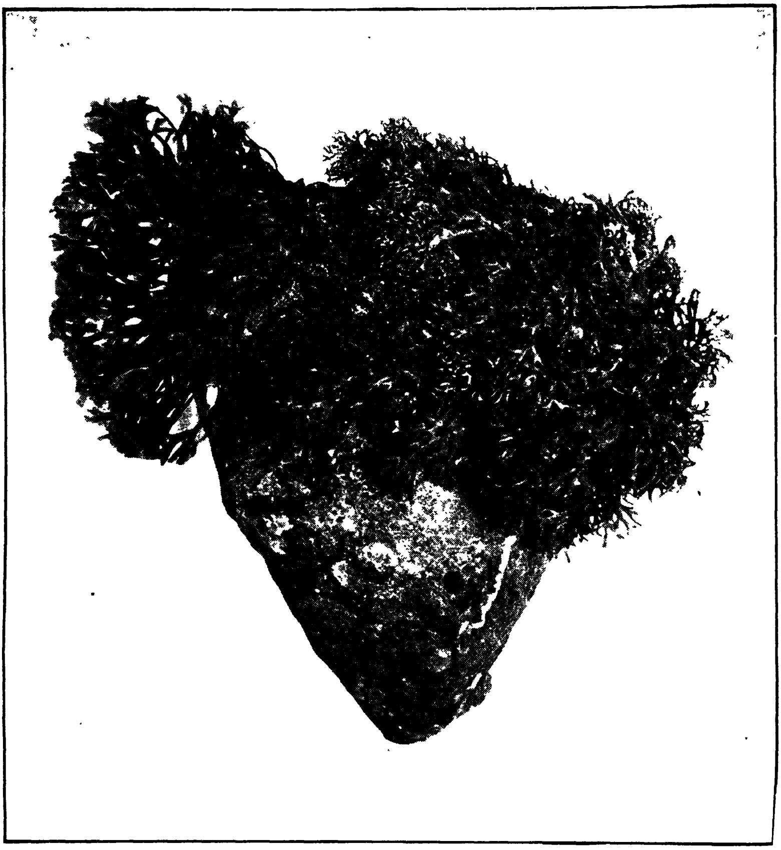


Fig. 27.—Specimen of *Chondrus crispus* attached to the rock where it was found growing along the Massachusetts coast.

These plants are common red algæ found along the northwestern coast of Ireland and the coast of Massachusetts. The plants are collected chiefly during June and July, spread out on the beach and bleached by the action of the sun and dew, then treated with salt water, finally dried and stored. The chief points of collection in this country are 15 to 25 miles south of Boston where *Chondrus crispus* is gathered. *Gigartina mamillosa* is most abundant north of the region where *Chondrus crispus* is collected and thus rarely occurs in the drug collected in the United States, though it is not unusual in the imported Chondrus.

Chondrus is an allusion to the cartilage-like character of the dry thallus; *Gigartina*, to the fruit bodies which appear as elevated tubercles on the thallus. The specific name *crispus* pertains to the curled fronds; *mamillosa* to the small breast-like, stalked fruit bodies or cystocarps.

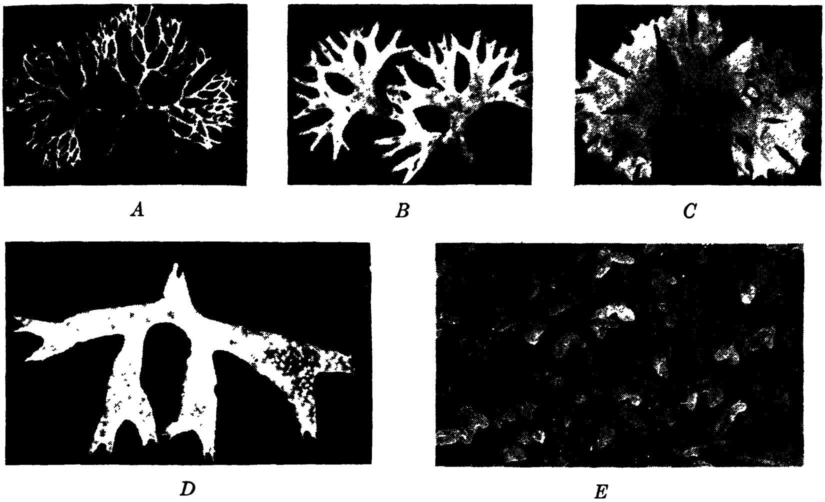


Fig. 28.—*Chondrus crispus.* *A*, Thallus with narrow segments; *B*, with broader segments; and *C*, with very broad segments. *Gigartina mamillosa*, *D*, natural size, showing many of the sporangia-bearing stalks, and *E*, somewhat magnified to show these branched, tubercle-like stalks projecting from the surface of the thallus. Photographs made from plants selected from commercial drug, moistened and spread out on glass. (Photo by Paul D. Carpenter.)

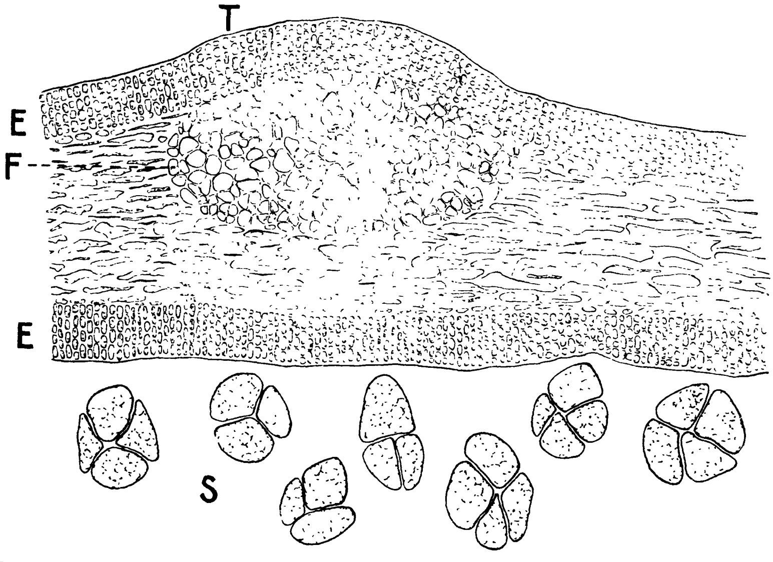


Fig. 29.—*Chondrus crispus.* Transverse section of thallus showing epidermis (*E*), sporangium with spores (*F*); *S*, spores separated in glycerin preparation of thallus by pressure on the cover-glass. The spores occur in groups of four (tetraspores) and the tetrad group is about 30 microns in diameter.

Description, Histology and Tests of Identification and Purity.—See Figures 27, 28 and 29 and the National Formulary.

Constituents.—From 55 to 80 per cent of carrageenin, a mucilaginous principle which is but slightly adhesive; about 10 per cent of proteins, and 10 to 20 per cent of total ash; the inorganic matter consists of calcium carbonate and compounds of sodium, potassium, magnesium and calcium with chlorine, iodine, bromine and sulfur.

Uses and Dose.—Chondrus is used as a demulcent, a nutrient and a dietetic. Its value as a nutrient has been questioned. Average dose, 10 gm. It is used also as an emulsifier and for thickening jellies. Both cold and hot water extracts of chondrus are used as a suspension agent in chocolate milk.

An artificial gum is prepared by adding starch to the mucilage of chondrus, and is said to be a good substitute for acacia, and may be employed as a base for fixing colors in fabrics.

EUMYCETES, OR TRUE FUNGI

The **True Fungi** comprise a multitude of lower plants of quite diverse structure. They are distinguished by the fact that they do not produce chloroplastids and hence are either parasitic or saprophytic. It has been estimated that the several groups comprise about 65,000 species. The economic relations of the fungi to life in general are of great importance, as they are largely responsible for the reduction of the complex compounds of dead organisms into the more simple compounds, such as carbon dioxide, water, nitrates and ammonium salts, which are utilized by photosynthetic plants to build again the foods necessary to maintain life. A few parasitic fungi may cause disease in plant and animal life.

A few fungi are edible and are even cultivated for this purpose. Others are exceedingly toxic and, unfortunately, may be gathered with some of the edible forms found growing naturally. Relatively few are used in medicine, but of these ergot is official in nearly all pharmacopœias.

Certain fungi, especially molds, produce during their growth on certain media powerful substances that destroy certain bacteria; penicillin and streptomycin are examples of these antibiotic substances. The antibiotics appear to be among the most valuable medicinal products and are being used as curative agents in many infectious diseases. (See page 78.)

SACCHAROMYCETACEÆ, OR YEAST FAMILY

Yeasts are unicellular organisms and are usually regarded as being greatly reduced sac-fungi. They feed upon sugars, splitting the latter to form alcohols and carbon dioxide; hence yeasts are of great importance in the alcohol industry and also in the making of bread, where the liberated carbon dioxide tends to swell the dough, making it porous and "light." Yeast is also used medicinally.

YEAST

The following titles of Yeast have been official: **Cerevisiæ Fermentum, Brewer's Yeast** (U. S. P. 1820 to 1831), **Fermentum, Brewer's Yeast**

(U. S. P. 1863 to 1882), **Cerevisiæ, Fermentum Compressum, Compressed Yeast** (N. F. 1916 to 1936; as a fermentative reagent, U. S. P. 1916 to 1936; N. F. 1916 to date), **Saccharomyces Siccum, Dried Yeast** (U. S. P. 1944 to date).

Brewer's Yeast is a viscid, semi-fluid, frothy mass containing the living cells of *Saccharomyces cerevisiæ*, or of other species of *Saccharomyces*, associated with bacteria and molds. Pure strains of yeast may be grown in suitable culture media containing sucrose and certain salts or proteins.

When yeast is grown at a temperature of 15° to 20° C. the cells are larger, tend to "bud" and form chains of cells and rise to the top of the fermenting mass. This is known as "top" yeast. If the temperature be kept near or below 10° C., the yeast cells are smaller, do not bud, apparently reproduce from spores, and the cells tend to remain in the lower portion of the fermenting mass and constitute "bottom" yeast.

Compressed Yeast is brewer's yeast or purer strains of yeast, partially dried by expression of water and admixed with a starchy or absorbent base. These yeast "cakes" wrapped in air-proof foil maintain the life of the yeast cells for a relatively long period of time.

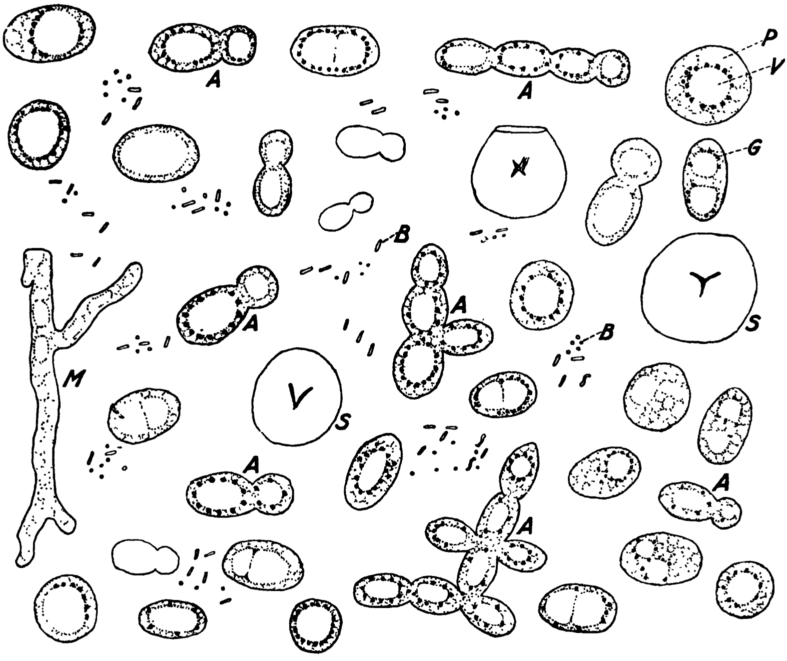


FIG. 30.—Yeast cells in compressed yeast and brewer's yeast. *A*, budding cells; *P*, protoplasm; *V*, vacuole; *G*, granules showing molecular motion; *M*, foreign mold; *B*, bacteria; *S*, cassava starch grains in yeast cake. (Drawing by Hogstad.)

Dried Yeast or Dry Yeast *(U. S. P. 1944 to date) consists of the dried* cells of any suitable strain of *Saccharomyces cerevisiæ* Meyen. Dry Yeast may be obtained as a by-product from the brewing of beer which has been made from cereal grains and hops. The yeast cells are washed free of beer, and may or may not be debittered. Dry Yeast also may be obtained by growing suitable strains of yeast, using media other than those required for the production of beer, and under appropriate environmental conditions. Yeast should be labeled to show its source as "Brewer's Dried Yeast," "Debittered Brewer's Dried Yeast" or "Primary Dried Yeast."

DESCRIPTION AND HISTOLOGY.—Dried Yeast occurs as yellowish white to weak yellowish orange flakes, granules or powder with an odor and taste characteristic of the type. As the yeast cells are dead, it is inactive in fermenting power. For a description of yeast cells see Figure 30 and the U. S. Pharmacopœia.

CONSTITUENTS.—Yeast contains a number of enzymes, including zymase, diastase and invertase; nucleoproteins; glycogen; and the growth-producing, antineuritic vitamin B.

STANDARDS.—Dried Yeast contains not less than 40 per cent of protein and in each gram, the equivalent of not less than 0.12 mg. of thiamin hydrochloride, 0.04 mg. of riboflavin and 0.25 mg. of nicotinic acid. The live bacteria count shall not exceed 7500 per gram and the mold count shall not exceed 50 per gram.

USES AND DOSE.—Dried Yeast is used almost exclusively for its vitamin contents. It has some repute as a laxative and occasionally is used for its food value. Average dose: 1 to 20 gm. daily according to the needs of the patient.

Concentrated or Dried Aqueous Yeast Extracts, prepared from specially cultured or brewer's dried yeast, are presented in liquid, powdered or tablet form.

HYPOCREACEÆ, OR FLESH-CONSUMING FAMILY

ERGOT

Ergot, Rye Ergot or Secale Cornutum (U. S. P. 1820 to 1947; N. F. 1947 to date) is the dried sclerotium of *Claviceps purpurea* (Fries) Tulasne, developed on rye plants.

Prepared Ergot or Powdered Defatted Ergot (N. F. 1947 to date) is ergot which has been powdered, immediately deprived of most of its fat, and dried.

The fungus has two distinct periods in its life history, an active and a resting stage. During the latter it forms a compact mycelium, or sclerotium, which replaces the flowers and grains of rye. The generic name *Claviceps* alludes to the club-like character of the sclerotium, *purpurea* to its purple color.

Ergot is picked by hand from the ears of rye, or it is separated after the threshing of the rye; it is carefully dried and preserved in rather tight containers against the attacks of insects by the use of small quantities of carbon tetrachloride or chloroform.

Ergot deteriorates when moist, even becoming moldy and rotten; it should be thoroughly dried, then kept dry in storage or transportation. The use of a cartridge of a non-liquifying, inert, dehydrating substance to maintain low humidity of the ergot, is desirable. Ergot deteriorates with aging, even though kept dry, yet well-preserved Prepared Ergot is known to have retained its therapeutic values for at least six years.

Description and Histology.—See Figures 31 and 32 and the National Formulary.

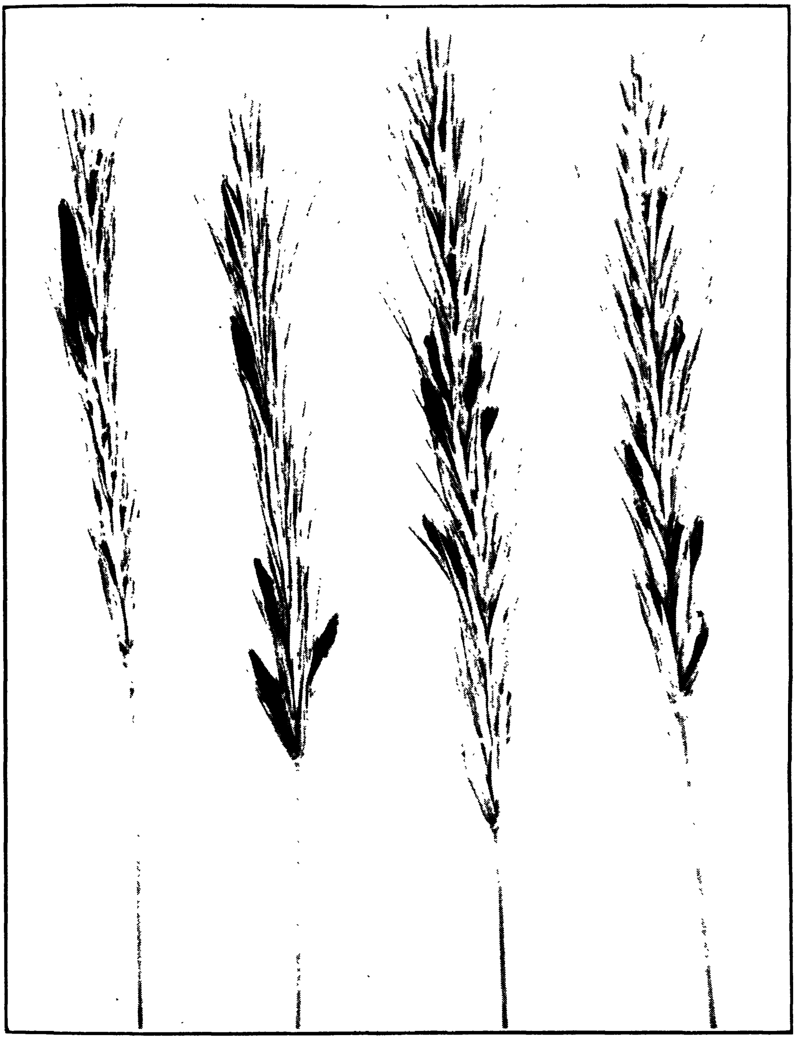


Fig. 31.—Ergot sclerotia developed in heads of the rye plant. (Photo by C. J. Zufall.)

Constituents.—Ergot contains several active alkaloids (see below) and amines, as well as amino-acids, coloring matter, sterols, glycosides, sugars, 30 to 35 per cent of fixed oil, etc.

Standards.—Ergot contains not more than 8 per cent of moisture, and Prepared Ergot not more than 6 per cent of moisture. For Tests of Identity and Purity see the National Formulary.

Uses and Dose.—Ergot is a vaso-constrictor and antihemorrhagic, and stimulant of uterine contractions in parturition. Average dose: 2 gm.; of Prepared Ergot, 0.3 gm.

Ergot Alkaloids:

Potent	Relatively inactive	Formula	Discoverer
Ergotoxine	Ergotinine	$C_{35}H_{39}O_5N_5$	Barger and Carr (1906)
Ergotamine	Ergotaminine	$C_{33}H_{35}O_5N_5$	Spira and Stoll (1920)
Ergosine	Ergosinine	$C_{30}H_{37}O_5N_5$	Smith and Timmis
Ergocristine	Ergocristinine	$C_{35}H_{39}O_5N_5$	Stoll and Burckhardt
Ergonovine	Ergometrinine	$C_{19}H_{23}O_2N_3$	Thompson, Kharasch, Dudley and Moir (1935)

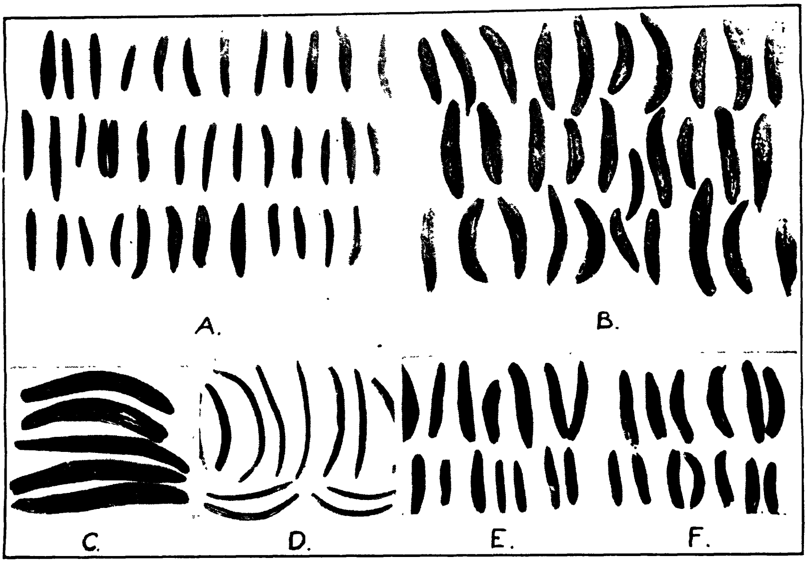


FIG. 32.—Ergota. *A*, Russian ergot; *B*, Spanish ergot; *C*, extra large Spanish ergot; *D*, Dyss ergot from Algeria; *E*, ergot of rye from Wisconsin; *F*, ergot of wheat. (About ½ natural size.) (Photos by Paul D. Carpenter.)

These alkaloids, in isomeric pairs, yield a common product, lysergic acid, and the isomerism is believed to occur in this part of the molecule. Other products of hydrolysis may differ for each pair of the alkaloids.

Ergotoxine Ethane Sulfonate (as reference standard: U. S. P. and N. F. 1936 to date) is used as a reference standard in the assay of ergot. It is official in the British Pharmacopœia. Ergotoxine occurs naturally in ergot. The salt is a white crystalline powder, sparingly soluble in water, freely soluble in alcohol or in a mixture of water and acetone. Its action is similar to that of ergot.

Ergotamine Tartrate (U. S. P. 1942 to date) occurs in colorless crystals or a white crystalline powder, sparingly soluble in water or in alcohol. For Tests of Identity and of Purity see the U. S. Pharmacopœia.

Ergotamine closely resembles ergotoxine in its oxytocic activity but is about one-half as toxic as the latter, as shown in the convulsive and lethal dosage for rabbits. The salt is remarkably effective for the symptomatic relief of migraine, usually within one hour. Average dose: intramuscular 0.5 mg., oral 1 mg.

Ergonovine Maleate (U. S. P. 1936 to date) occurs as a white or faintly yellow, odorless microcrystalline powder, affected by light, readily soluble in water, less soluble in alcohol. The alkaloid was discovered by three groups of independent workers, and announced almost simultaneously in 1935. Because of its ready solubility in water, this alkaloid has marked advantages over the other ergot alkaloids. The oxytocic effect of the drug either orally or subcutaneously is sometimes noted within five minutes after giving the dose, and its effect is more marked than that of either ergotoxine or ergotamine. However, *the vasoconstrictor effect is much less marked. Average dose: intravenous or intramuscular 0.2 mg.; oral, 0.5 mg.*

Ergot Amines:

Ergot contains at least two potent amines; namely, Histamine and Tyramine

Histamine Phosphate or Histamine Acid Phosphate (U. S. P. 1936 to date) is a phosphate of *b*-iminazolylethylamine. It is found in ergot, apparently as a decomposition product of histidine, though it is usually obtained from certain putrid meat products and may be classed as a ptomaine. The salt occurs as colorless, odorless, long prismatic crystals, soluble in about four parts of water. For Tests of Identity and Purity see the U. S. Pharmacopœia.

Histamine Phosphate reduces blood pressure and is a powerful stimulant of the excised uterus. Average dose: 0.3 mg.

Histidine Monohydrochloride (N. F. 1947 to date) occurs as small, glistening, colorless crystals, nearly odorless and with a salty taste. It is readily soluble in water and in alcohol. For Tests of Identity and Purity see the National Formulary.

Histidine is an indispensable amino acid and may be broken down to yield histamine. The known pharmacologic effects of histidine are relatively slight; it is reputed to have a marked effect on the relief of gastric ulcers. Average dose: 0.2 gm.

Tyramine is closely related to epinephrine in chemical structure and in pharmacologic action, though it is much less powerful than epinephrine, and more closely resembles the action of ephedrine. It is mainly responsible for the pressor effect of ergot.

Ergosterol, found in ergot oil and in certain other oils, is the only known substance to give rise to vitamin D upon irradiation with ultra-violet light (see page 667).

Ustilago or Corn Smut (U. S. P. 1882 to 1894) is the fungus, *Ustilago zeæ* (Fam. *Ustilaginaceæ*) developed upon the stems and flowers of the Indian corn (*Zea mays*). It occurs in irregular, somewhat cylindrical or globose masses from 10 to 15 cm. in diameter, consisting of a whitish membrane, becoming dark with age, and a brownish black mass of spores, the latter nearly spheroidal and about 7 microns in diameter. The drug has a heavy odor and a disagreeable taste. Ustilago should be carefully dried and kept not longer than one year.

Corn smut contains a crystallizable alkaloid, ustilaginine, which is soluble in water and in alcohol, and forms crystalline salts; a crystallizable substance, maizenic acid, which resembles sclerotic acid; a volatile base resembling trimethylamine; fixed oil; two resins, one alcohol-soluble, one ether-soluble; a non-reducing sugar; and yields about 4.5 per cent of ash.

Corn smut has been used medicinally somewhat like ergot but is weaker and of lower toxicity.

Agaric, White Agaric or Larch Agaric (N. F. 1916 to 1936) is the dried fruiting body of the fungus *Polyporus officinalis* (Fam. *Polyporaceæ*), deprived of its outer rind.

The commercial supplies are obtained from the mountainous regions of Southern Europe and Siberia, the product being collected from larch trees.

Agaric occurs in light, spongy, irregular pieces, mostly 8 to 14 cm. in diameter; externally yellowish white to yellowish brown and showing at places the characteristic porous surface so common in the genus; easily cut, having a corky texture; internally whitish or light brown with yellowish striations and sometimes a smooth shiny surface, and occasionally with pieces of larch wood embedded; odor aromatic; taste slightly aromatic, acrid and intensely bitter.

The drug contains about 50 per cent or more of resin consisting of four resinous substances: α-resin, reddish, bitter and pungent; β-resin or agaricinic acid, the most important principle, forming yellowish crystals which are slightly soluble in water and ether and very soluble in boiling water or hot alcohol; γ-resin, 3 to 4 per cent, amorphous; δ-resin, soft and in small quantities. It also contains a fatty substance, a nitrogenous substance, mannite, tannic acid, phosphoric acid, malic acid, tartaric acid, oxalic acid, cellulose from 10 to 30 per cent, and ash from 1 to 2 per cent, the latter particularly high in phosphorus.

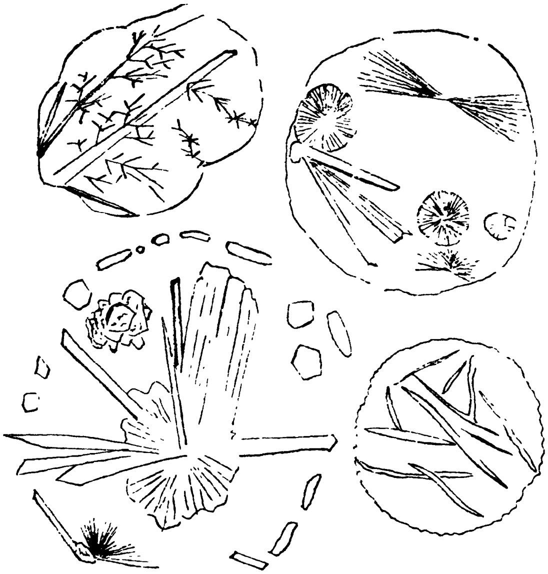


Fig. 33.—Sublimate crystals obtained by heating small quantities of powdered *Polyporus officinalis*. The crystals resemble those of agaricinic acid. The sublimate consists first of slightly colored globules, in which on drying there separates needles or needle aggregates and in some cases large plates, which are strongly polarizing and show extinction parallel with the long axis. (After Tunmann.)

Agaric yields not less than 50 per cent of non-volatile extractive, when treated with boiling alcohol.

Agaric and agaricinic acid possess antidiaphoretic properties, being fully equal to atropine in the effect of suppressing dermic action. Average dose: 0.6 gm.

Surgeon's Agaric, or Boletus Ignarius (U. S. P. 1831 to 1842, N. Y. edition) grows on beech and oak trees in Central and Southern Europe up to 30 cm. broad and 10 cm. thick at the tree. The fungus is deprived of its hard rind, cut into thin slices, boiled in weak lye, washed, and beaten with mallets until soft. It is then of a cinnamon-brown color, glossy, soft and velvety. It was used by surgeons for absorbing body fluids, blood, etc., which could then be washed out and the agaric dried for further use. When antisepsis became known, the use of agaric for this purpose ceased.

Poisonous Fungi.—On account of the high protein content in some of the edible fungi, varying from 20 to 60 per cent in the dried material of *Agaricus campestris*, considerable interest has been shown, especially in foreign countries, in teaching the citizens the food value of these mushrooms. Persons who make it a practice to gather edible mushrooms should know what to gather, for numerous serious cases from the eating of poisonous fungi are reported every year. The pharmacist may be called upon to identify the species which has been the cause of poisoning. A very excellent Bulletin has been prepared by Flora W. Patterson and Vera K. Charles of the Bureau of Plant Industry, U. S. Department of Agriculture, entitled, "Mushrooms and Other Common Fungi."

LICHENES, OR LICHENS

Lichens are a peculiar group of plants, composed of certain of the higher fungi parasitic upon one of the green or blue algæ. They are of rather common occurrence upon the barks of trees and rocks, and some grow upon soil. They consist of a thallus in which the algal cells have a more or less definite position. (See Fig. 34.)

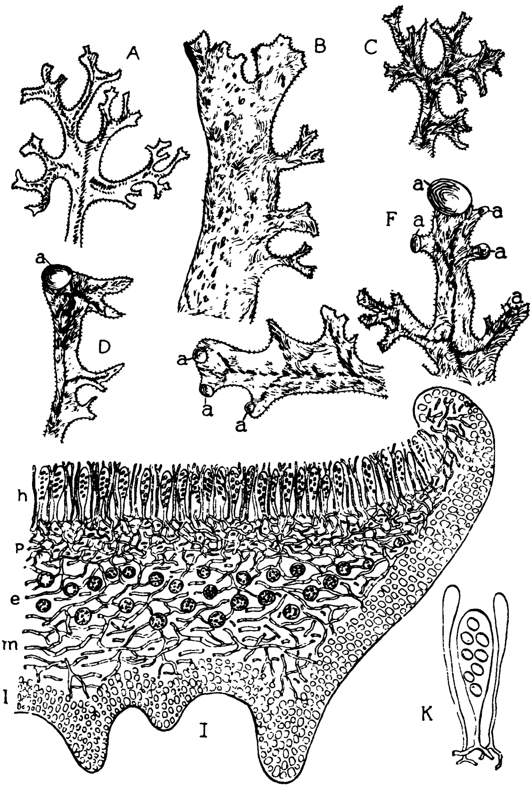


Fig. 34.—Iceland moss (*Cetraria islandica*). *A*—*F*, Various forms of thalli showing apothecia (*a*); *I*, cross-section of an apothecium showing the hymenium (*h*); the hypothecium (*p*), the algal layer (*e*), the medullary layer (*m*), and lower or ventral surface (*l*); *K*, an ascus with eight ascospores and two paraphyses from the hymenium (*h*).

Many lichens contain lichenin, a carbohydrate resembling starch, hence they have a certain food value and a few have been used as food. While some are of medicinal interest their chief interest is in the coloring principles which they contain and which have been the subject of painstaking investigations by O. Hesse during many years.

Cetraria or Iceland Moss (U. S. P. 1820 to 1905) is the entire dried plant of *Cetraria islandica* (Fam. *Parmeliaceæ*), which is widely distributed over the northern part of both hemispheres. The chief commercial supplies are obtained from Scandinavia, Germany, Switzerland and parts of Austria.

Cetraria consists of a number of somewhat dichotomously branching, more or less curled, papery, fringed segments, 5 to 10 cm. long and about 5 mm. wide. The upper surface is greenish brown, with occasional dark reddish brown cupular apothecia, and the under surface grayish, with numerous small, whitish, depressed spots. It is tough when damp, but brittle when dry. It has a slight odor and a mucilaginous and bitter taste.

Cetraria contains lichenin and isolichenin (about 70 per cent); the former is like soluble cellulose, for the hot aqueous solution gels upon cooling but is not colored blue with iodine; the latter is like soluble starch, the cold aqueous solution giving a blue reaction with iodine; cetrarin, a bitter crystallizing principle, yielding on hydrolysis cetraric acid, which is also intensely bitter; lichenostearic acid; several organic acids including fumaric or lichenic acid; cellulose; sugar; gum; thallochlor, resembling chlorophyll; and yields less than 2 per cent of ash.

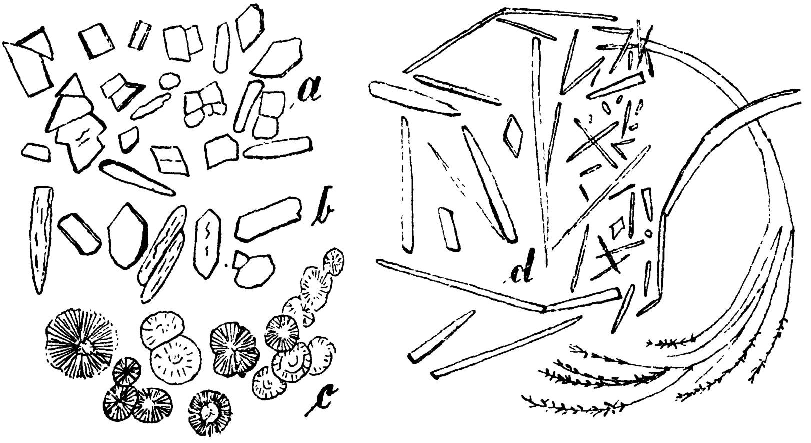


FIG. 35.—Crystals of lichenostearic acid obtained by microsublimation of pieces of the thallus of Cetraria, not larger than 0.5 cm. square. *a*, Crystals obtained by sublimation; *b*, a granular sublimate which was recrystallized from alcoholic solution; *c*, sublimate treated with sodium carbonate and showing crystal aggregates of the sodium salt of lichenostearic acid; *d*, sublimate treated with ammonia giving crystals of the ammonium salt of lichenostearic acid. (After Tunmann.)

The bitter principle in cetraria may be removed by treating the drug with a 1 per cent solution of potassium carbonate at about 60° C. for several hours.

Iceland moss jelly is prepared by making a decoction of 3 parts of washed cetraria and 100 parts of water, adding 3 parts of sugar and evaporating the whole to 10 parts. **Dried saccharated Iceland moss** is prepared somewhat similarly to the Iceland moss jelly, but the product is evaporated to dryness and then powdered.

Cetraria is a demulcent and nutrient. Average dose, 10 gm. in the form of a decoction.

Allied Plants.—Lichens of allied families also yield sugars: *Usnea barbata* and *Cornicularia aculeata* contain a principle resembling lichenin, which on hydrolysis yields glucose. *Evernia prunastri* contains a carbohydrate, evernin, which resembles lichenin but is dextrogyrate. *Cladonia rangiferina* contains 30 per cent of mannose; *Stereocaulon paschale* and *Peltigera aphthosa* yield on hydrolysis dextromannose and dextrogalactose.

ORCHIL, LITMUS AND CUDBEAR

Orchil or Archil is a coloring substance obtained by the fermentation of *Roccella tinctoria*, *R. fuciformis* and other lichens (Fam. *Roccellaceæ*). *R. tinc-*

toria is abundant in the Levant, the Canary Islands and the Cape Verde Islands, while *R. fuciformis* is quite common on the islands of the Indian Ocean adjoining the African coast. The lichens grow on the rocks near the sea and after being cleansed they are ground into a pulp with water. They are then treated with some ammoniacal liquid, such as dilute solution of ammonia and allowed to ferment for nearly a week.

Orcinol (as reagent; U. S. P. 1916 to 1926; N. F. 1942 to date) is obtained from certain lichens by fermentation of orchil, or is prepared synthetically.

Orcinol occurs as colorless, monoclinic crystals, soluble in water, alcohol and ether. Orcinol is converted by alkaline fermentation to orcein which produces scarlet solutions with either water or alcohol. Orcein is readily soluble in alcohol, somewhat soluble in water, and insoluble in ether. It forms beautiful lavender-colored solutions with the alkalis.

Litmus (as reagent: U. S. P. 1926 to 1936, 1942 to date; N. F. 1942 to date).

Litmus Test Solution (U. S. P. 1882 to 1926, 1942 to date; N. F. 1936 to date).

Red and Blue Litmus Paper (U. S. P. 1882 to date; N. F. 1936 to date).

Azolitmin (U. S. P. 1916 to 1926; 1942 to date; N. F. 1936 to date).

Litmus, Lacmus, Turnsole or Lacqueblue is a blue pigment prepared from various species of *Roccella*, *Lecanora* or other lichens (Fam. *Parmeliaceæ*).

The process of fermentation is similar to that in the preparation of orchil and cudbear, but potassium carbonate is added and the time of fermentation is longer. When the color of the solution is of the desired tint it is mixed with calcium carbonate or gypsum, molded into small cubes and finally dried. Most of the litmus is manufactured in Holland.

DESCRIPTION.—Litmus occurs in cubes, masses, fragments or granules of an indigo blue or deep violet color. It has a somewhat fragrant odor and a pungent, saline taste tinging the saliva a deep blue. The indicator substances contained in litmus are soluble in water and less soluble or insoluble in alcohol. For TESTS and STANDARDS see the National Formulary.

Azolitmin is a water-soluble coloring matter obtained from litmus, it occurs in dark violet scales, easily soluble in hot water and in dilute alkalis, forming a deep blue solution.

Cudbear (N. F. 1916 to date) is a powder prepared from species of *Roccella* DeCandolle, *Lecanora* Acharius, or other lichens (Fam. *Parmeliaceæ*).

Cudbear is prepared in much the same manner as orchil. The coloring principle is apparently orcein. Cudbear is used as a coloring agent for pharmaceutical preparations as well as in dyeing.

DESCRIPTION.—Cudbear occurs as a very dusky red or red-purple powder, showing under the microscope fragments of hyphæ and pseudo-parenchyma from the lichen, but very little woody or leafy tissue.

STANDARDS.—Cudbear, extracted with water or with alcohol, forms a deep red solution which is rendered lighter in tint by the addition of acids, and is changed to purplish-red on the addition of alkalis. For further standards see the National Formulary.

BRYOPHYTA OR BRYOPHYTES

The **Bryophytes** (from two Greek terms meaning "moss plants") include the liver-worts and the true mosses. They show a true alternation of generations; *i. e.*, the sporophyte, or asexual form and the gametophyte or sexual form. The sporophyte tends to show a differentiation into stems, leaves and root hairs, which absorb soil solutes and serve as holdfasts. The plants are chlorophyll-bearing, hence are neither saprophytic nor parasitic. There are about 3000 species of mosses, widely scattered in all climates and under many soil conditions, though they generally require an abundance of moisture.

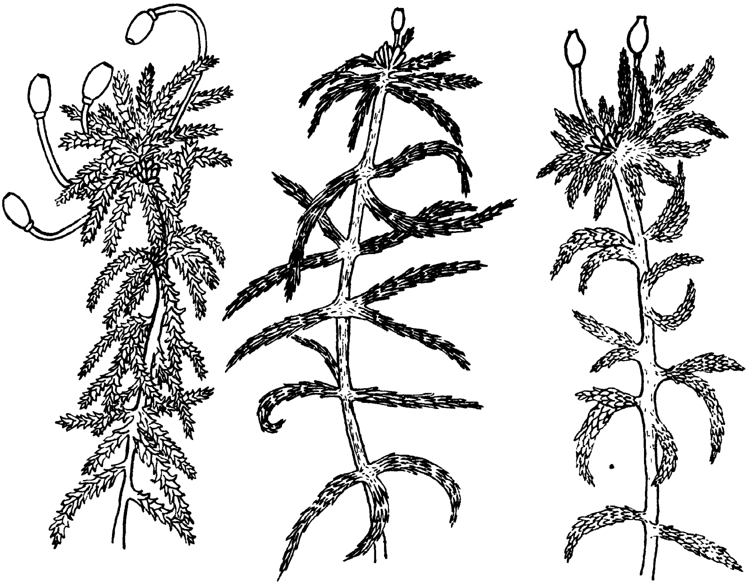


FIG. 36.—Left, *Sphagnum squarrosum;* center, *Sphagnum acutifolium;* right, *Sphagnum cymbrifolium.* (Drawing by Edward Fried, University of Illinois, College of Pharmacy.)

The **Sphagnum** mosses serve a great economic purpose in that the thick beds and large areas of water-absorbent plant material, produced by succeeding generations of these plants, accumulate the excessive moisture of the rainy season and hold this water in reserve to supply the streams in the dry season. Such peat beds, when cut into suitable masses and dried, serve as fuel. This moss is also used for packing living plants for shipment. The shredded, cleaned and dried sphagnum moss is utilized for absorptive purposes. It is more absorptive than prepared cotton and, in the form of pads, serves many useful purposes.

PTERIDOPHYTA OR PTERIDOPHYTES

The **Pteridophytes** include the ferns (*Filicales*), the horsetails or scouring-rushes (*Equisetales*), and the club mosses or lycopodiums (*Lycopodiales*).

The *Pteridophyta* constitute a very old group of plants, being first found in the Devonian and attaining their maximum development in the Carboniferous age, during which time they formed the bulk of the vegetation comprised in the coal measures. The existent forms are still numerous, exceeding 5000 species. Their chief economic value lies in their use as ornamental plants.

EQUISETALES

The *Equisetaceæ* or Horsetail Family is the only family of this order. It furnishes but little of medicinal value.

Equisetum is the herb of *Equisetum arvense*, Field Horsetail, or of *E. hyemale*, Scouring-rush; these have been used medicinally, mostly as diuretics. The former plant contains equisetic acid, possibly identical with aconitic acid.

Other species of *Equisetum* contain the alkaloid equisetine, which is destructive to cattle. Certain other species have been used as intestinal and urethral astringents.

FILICALES

The *Filicales* or true ferns are widely scattered, and comprise more than 4000 living and 900 known fossil species, the living species being classified into 9 families. Practically all of our common ferns belong to the families *Polypodiaceæ* and *Osmundaceæ*.

The *Filicales* possess a stem, usually an underground creeping stem or rhizome, which bears roots below and fronds above. The fronds consist of a petiole or stipe and an expanded lamina, often lobed or divided into pinnæ. The sporangia often develop on the under surface of the lamina, but sometimes the whole lamina becomes a spore-bearing organ. The sporangia frequently are clustered in a sorus, a small, circular, brownish swelling which eventually breaks open and scatters the spores. The spore falling into a moist and shady spot will develop into the gametophyte, a flat, green prothallus, which bears the sexual spores on the underside adjacent to the earth. Cross fertilization occurs by means of the water currents and a chemotactic influence. After fertilization, a new plant develops and this sporophyte becomes the typical fern plant.

POLYPODIACEÆ, OR POLYPODIUM FAMILY

ASPIDIUM

Aspidium (U. S. P. 1831 to date) consists of the rhizome and stipes of *Dryopteris Filix-mas* (Linné) Scott (U. S. P. 1831 to date), known in commerce as European Aspidium or Male Fern, or of *Dryopteris marginalis* (Linné) Asa Gray (U. S. P. 1882 to 1916, 1942 to date), known in commerce as American Aspidium or Marginal Fern.

Dryopteris Filix-mas is a perennial wood fern, widely distributed, being indigenous to Europe, Asia, North America west of the Rocky Mountains, and the Andes of South America. *Dryopteris marginalis* is found in the Eastern and Central United States and north to Prince Edwards Island. The drugs are collected in early autumn and trimmed to leave the lower portions of the stipes attached to the rhizome; or the stipes are separated from the rhizome and the dark brown periderm removed. The drug should be carefully dried and preserved.

The generic name *Dryopteris* is from the Greek meaning a fern growing on oaks; the specific name *filix-mas* means "male fern" in reference to its asexual fructification; the specific name *marginalis* pertains to the marginal position of the sori in this species.

DESCRIPTION AND STRUCTURE.—See Figure 37 and the U. S. Pharmacopœia

CONSTITUENTS.—Ether extracts 6.5 to 15 per cent of oleoresin from the drug, which contains the active principle, namely amorphous filmaron, a complex dibasic acid, and amorphous filicic acid. Filicin or crystalline filicic acid may be an anhydride of amorphous filicic acid. Only the amorphous acidic compounds are considered to be anthelmintic. The drug also contains fixed oil, tannic acid, several resins, sugar, and about 2.7 per cent of total ash.

STANDARDS.—Aspidium contains not less than 1.5 per cent of crude filicin. The acid-insoluble ash is not more than 3 per cent.

USES AND DOSE.—Aspidium is an anthelmintic used in the treatment of tape-worm, usually administered as a single dose of about 4 gm. of the oleoresin. It should be preceded and followed by a laxative, saline cathartics being preferred, as it is claimed that castor oil increases the absorption of filicic acid, which is dangerous when absorbed in large amounts. In case the treatment fails, ten days or more should elapse before a second administration.

ADULTERANTS.—The rhizomes of other ferns are sometimes substituted for those of the true drug, such as that of *Osmunda claytoniana* and related species. These occur in large pieces with coarse, wiry roots, and flattened stipes and free from chaffy scales.

The rhizome of *Dryopteris spinulosa* (Shield Fern) appears to possess properties similar to the official drug; it somewhat resembles that of *D. filix-mas*, but the chaffy scales possess marginal glandular hairs and the number of fibro-vascular bundles in the rhizome is usually but 6 or 7. The rhizome of the **Lady Fern**, *Athyrium filix-fœmina* has also been found as an adulterant.

The rhizome of *Pteridium aquilinum* contains a cyanogenetic amygdalin-like glucoside.

Polypodium (U. S. P. 1820 to 1831) is the rhizome and roots of *Polypodium vulgare*. The drug apparently contains no filicic acid and has no tænifuge activity.

Adiantum, Maidenhair or Venus Hair consists of the fronds of *Adiantum pedatum* or *A. capillus-veneris*. These well-known ferns are rather common in Eastern and Central United States and are occasionally used in medicine as demulcents, expectorants and tonics. The value of this medicinal use is open to question. They are among the most graceful and delicate of the North American ferns. The rhizomes are horizontal, slender and with blackish roots. The leaves are few but well developed in the early part of the summer. They consist of long, blackish and shining petioles, pedately branching at the summit, first into two recurving, primary forks, and then into several spreading divisions, each of which bears numerous regularly alternating leaflets. The latter are obliquely triangular-oblong, the upper margin being incisely lobed and serrate;

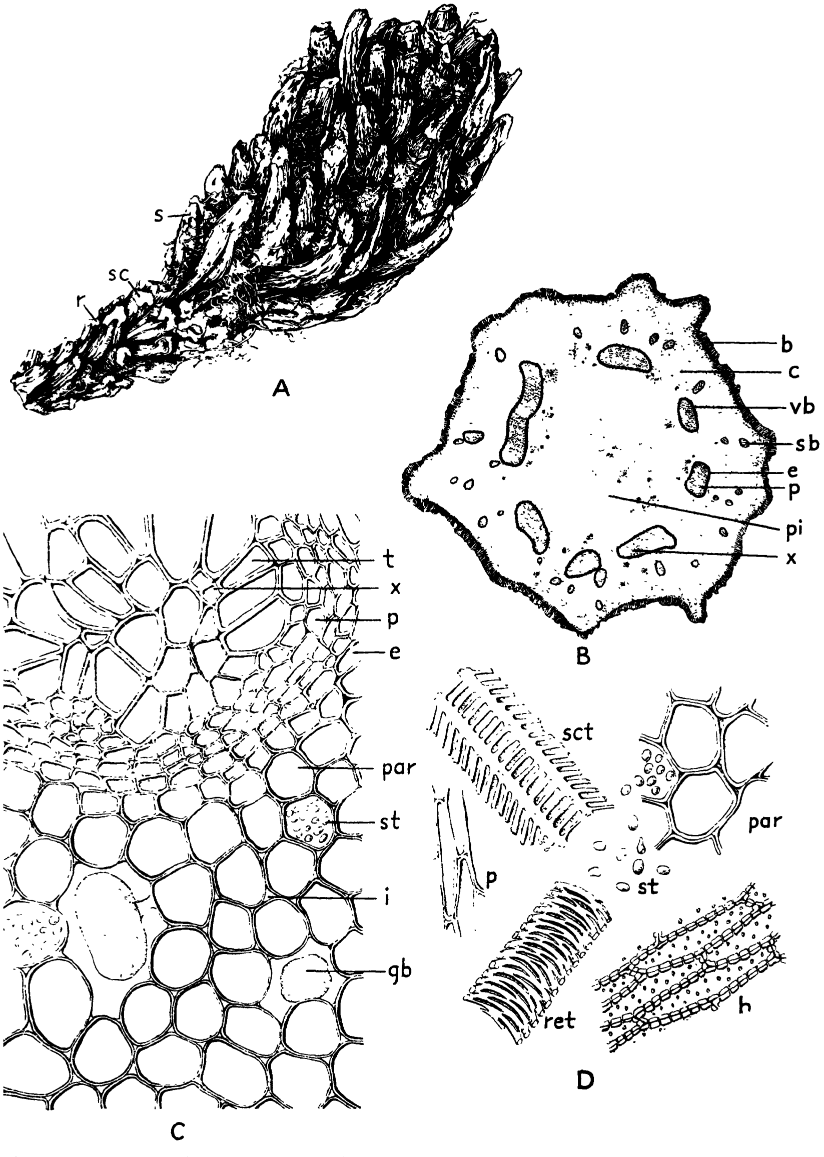


Fig. 37.—*Dryopteris filix-mas.* A, Rhizome (*r*) with stipe scars (*sc*) and attached stipes s). *B*, Lens view of a transverse section of the rhizome showing hypodermis (*b*), cortex), stipe-trace bundles (*sb*), concentric vascular bundles (*vb*) each surrounded by an ndodermis (*e*) and showing a central xylem (*x*) and a surrounding phloem (*p*). *G*, ransverse section of the fundamental parenchyma including a portion of a bundle, owing xylem (*x*) with large tracheæ (*t*), phloem (*p*), endodermis (*e*), parenchyma (*par*) ntaining starch (*st*) and exhibiting intercellular spaces (*i*) and the internal glandular airs (*gb*) containing the oleoresin. *D*, Principal elements of the powder; scalariform acheæ (*sct*); reticulate tracheæ (*ret*); porous, lignified hypodermal cells (*h*); phloem cells); and cells of the fundamental parenchyma (*par*) containing ovoid, oblong, ellipsoidal r irregular starch grains (*st*) up to 25 microns in diameter. (Drawings by Marder and irth.)

the surface is glaucous and very smooth. The odor is slight, the taste being slightly bitter and somewhat astringent. For the structure consult Holm, Merck's Report, 1909, page 62.

LYCOPODIALES

The clubmosses differ widely from the ferns and horsetails in both sporophytic and gametophytic characteristics. Many fossil forms, larger and more complicated in structure than any living forms, are known. The living clubmosses are mostly tropical, but some are widely distributed in the temperate regions. Two families are included: *Lycopodiaceæ* and *Selaginellaceæ*.

LYCOPODIACEÆ, OR CLUBMOSS FAMILY

But two genera, *Lycopodium* and *Phyloglossum* are included in this family.

The *Lycopodiums* (about 100 species) are perennial herbs found over most of the globe. They possess a herbaceous, creeping or pendant, somewhat branching stem. The leaves are small, lanceolate, sessile, evergreen, and arranged spirally around the stem, or in four ranks with the opposite leaves on the flattened sides of the stem somewhat larger, and those on the edges, smaller. The fruiting bodies are strobiles with green leaf-like scales (*L. selago*), or smaller yellow scales on a thin upright branch (*L. clavatum*).

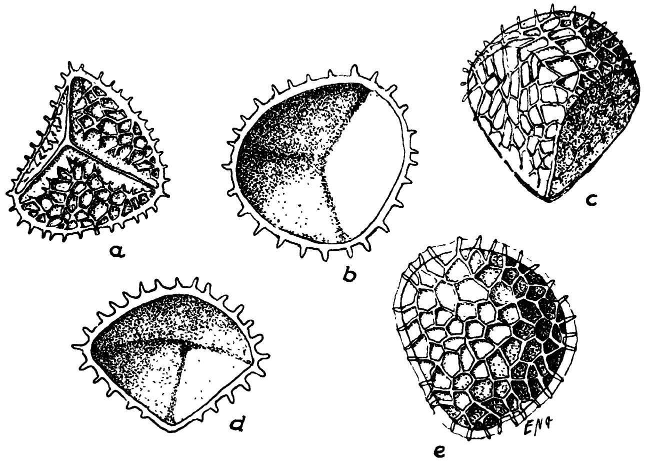


FIG. 38.—Spores of *Lycopodium clavatum*, showing markings in the form of protuberances on the cell wall. *a*, *c*, and *e*, the whole spores; *b* and *d* sectioned spores showing the interior but without cell contents. (Drawings by Gathercoal.)

LYCOPODIUM

Lycopodium (U. S. P. 1863 to 1947; N. F. 1947 to date) consists of the spores of *Lycopodium clavatum* Linné. The spores are obtained from the ripened cones by shaking the fruiting tops on cloths, and the extraneous matter is removed by sifting. The principal sources of supply are Esthonia, Latvia, Western Russia and Switzerland.

The generic name *Lycopodium* is derived from the Greek and has reference to the fancied resemblance of the shoots of the plant to the foot of a wolf; the specific name *clavatum* refers to the club-like character of the strobile.

DESCRIPTION.—A light-yellow, very mobile powder, nearly inodorous and tasteless, floating upon water and not wetted by it, but sinking on being boiled with it, and burning quickly when thrown into a flame. The spores are somewhat like a three-sided pyramid with convex base, from 25 to 40 microns in diameter; the outer surface reticulate, the reticulations being polygonal and formed by straight-sided delicate ridges which form a delicate fringe at the edges of the spore; when viewed with the rounded surface of the spore on the under side, a distinct triangular marking is seen, formed by the edges of the flat surfaces of the spore.

CONSTITUENTS.—About 50 per cent of a deep green odorless, non-drying oil with an acid reaction, which consists chiefly of oleic acid. The spores yield about 1 per cent of ash. On heating with a solution of potassium hydrate, monomethylamine is liberated, and on macerating the spores in alcohol, a part of the alcohol is converted into an aldehyde.

USES.—Lycopodium is used as a dusting powder to protect tender surfaces and as an absorbent. In pharmacy it is used to prevent the adhering of pills and suppositories.

ADULTERANTS.—Lycopodium is sometimes admixed with pine pollen, starchy materials, and various inorganic substances, as sulfur, talc and gypsum. A recent adulterant of lycopodium has been found to consist of corn starch which had been treated in a special manner and then colored with methyl orange. An artificial lycopodium is prepared by treating Bordeaux turpentine (galipot resin) at near the melting-point with dry ammonia, the resulting product being then dried and powdered. The fragments are irregular and transparent and are detected by means of the microscope.

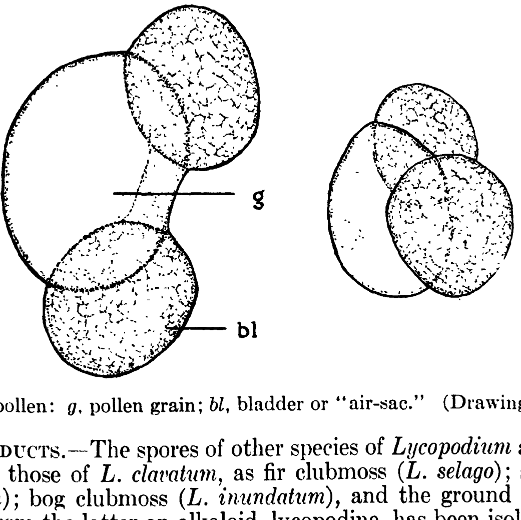


FIG. 39.—Pine pollen: *g*, pollen grain; *bl*, bladder or "air-sac." (Drawing by Adamson.)

ALLIED PRODUCTS.—The spores of other species of *Lycopodium* are sometimes collected with those of *L. clavatum*, as fir clubmoss (*L. selago*); stiff clubmoss (*L. annotinum*); bog clubmoss (*L. inundatum*), and the ground pine (*L. complanatum*). From the latter an alkaloid, lycopodine, has been isolated. A toxic alkaloid, piliganine, has been obtained from piligan (*L. saururus*), growing in Brazil. *L. polytrichoides*, of the Hawaiian Islands; *L. rubrum*, of Venezuela; *L. cernum*, of the Tropics, and *L. selago*, of Europe, are also employed in medicine.

SPERMATOPHYTA OR SPERMATOPHYTES

The Spermatophytes (seed-bearing plants) represent the most complex types of the plant kingdom. They are mostly chlorophyll-bearing, with but very few parasitic or saprophytic forms; they usually produce well differentiated roots, stems, leaves, and flowers, and, by sexual fertilization, seed. The seed may be produced on exposed bracts (the Gymnosperms) or in closed carpels (the Angiosperms). The number of species, approximately 133,000, probably is greater than is found in all other groups of plants. Most of our vegetable drugs come from the Spermatophytes.

GYMNOSPERMÆ OR GYMNOSPERMS

This is an ancient order of plants which arose in the Devonian and reached its zenith in the Carboniferous Period. It was especially predominant during the Triassic Age. The surviving forms are represented by about 650 species, divided into the *Cycadales*, *Ginkgoales*, *Coniferales* and *Gnetales*.

CYCADALES OR CYCADS

Only a single family, the *Cycadaceæ*, including 9 genera and about 100 species, constitutes this order. It yields no medicinal products of importance, but several economic products of value. These plants possess a thick, unbranched, cylindrical stem, sometimes very short, but again reaching a height of 60 feet. The leaves, usually pinnately compound, are borne spirally around the stem, leaving, as they decay, the bases of the petioles covering the stem; in older plants, the leaves form a crown at the top of the stem.

The sago palms, species of *Cycas*, furnish an important economic product, namely, the starch found in the stem, which constitutes **Sago.** (See pages 120 and 148.)

GINKGOALES

Only a single species, *Ginkgo biloba*, widely cultivated as an ornamental tree, but native to China, is found in this order. The leaves are not "evergreen" or needle-shaped, but drop at the end of the growing season and are broadly fan-shaped. In structure, the stem resembles the Conifers and in fruit-bearing, the Cycads.

CONIFERALES OR CONIFERS

The Conifers (cone-bearing) include several families, 46 genera and about 500 species. The plants are mostly resinous trees or shrubs, with stems which possess a pith, a circle of open collateral bundles, and a true bark. The leaves are evergreen, usually sessile and either narrow, linear or needle-shaped, or flat and scale-like. The fruits are cones usually with woody bracts but sometimes fleshy.

The Conifers are of great economic importance for their timber and for ornamental purposes, as well as for many valuable resinous or oleoresinous products, which include the natural oleoresins, obtained as natural exudations or by incising the trunks; the volatile oils and resins, obtained by distillation of the oleoresins; the "tars" and "pitches," obtained by destructive distillation of the wood or the resin; and the volatile oil (especially from the leaves) obtained by steam distillation. These plants also yield valuable tanning barks, medicinal barks, medicinal fruits and, in some instances, seeds used for human food.

Plant Products from the Coniferales

Because this group of plants is noted for its resinous products, a general discussion of these products will be presented at this point.

Resins probably never occur free in plants but are associated with other plant products, such as volatile oils, gums, benzoic acid, cinnamic acid, or small amounts of other substances.

Resinous plant products are produced normally during growth or are secreted as a result of injury to the plant. They usually occur in cells, sacs or canals especially formed by the plant for the purpose of holding them. Resins occur in 33 families of the Spermatophytes.

RESINS

When resins are separated and purified they are usually brittle, amorphous solids which fuse readily upon heating, after passing through a preliminary stage of softening. They are insoluble in water, but dissolve in alcohol or other organic solvents, forming solutions which, on evaporation, deposit the resin as a varnish-like film. Resins burn with a characteristic, smoky flame.

Resins may be considered as final products in destructive metabolism. Many are believed to be oxidation products of the terpenes. They are usually more or less complex mixtures and their principal constituents may be classified as follows:

Resin Acids.—These contain a large proportion of oxy-acids, usually combining the properties of carboxylic acids and phenols. They occur both in the free state and as esters. They are soluble in aqueous solutions of the alkalies, usually forming soap-like solutions or colloidal suspensions. Their metallic salts are known as resinates, and some of these are used extensively in the manufacture of cheap soaps and varnishes. Examples of these are abietic acid in rosin or colophony, copaivic and oxy-copaivic acid in copaiba, guaiaconic acid in guaiac, pimaric (pimarinic) acid in Burgundy pitch and frankincense, sandaracolic (sandaracinolic) acid in sandarac, aleuritic acid in shellac, and commiphoric acid in myrrh.

Resin Alcohols.—Complex alcohols of high molecular weight, known as **resinotannols**, are those which give a tannin reaction with iron salts; and **resinols**, those which do not give such a reaction. The resin alcohols occur in the free state and as esters in combination with simple aromatic acids (benzoic, salicylic, cinnamic, umbellic). The following resinotannol resins have been isolated: aloeresinotannol from aloes, ammoresinotannol and galbaresinotannol from ammoniac, peruresinotannol from balsam of Peru, siaresinotannol and sinnaresinotannol from benzoin, and toluresinotannol from balsam of tolu. The following are examples of resinol resins: benzoresinol from benzoin, storesinol from styrax, gurjuresinol from gurjun balsam, and guaiacresinol from guaiac resin.

Resenes.—Complex neutral substances devoid of characteristic chemical properties. They do not form salts or esters, and are insoluble in and resist hydrolysis by alkalies. They include alban and fluavil from gutta percha, copalresene from copal, dammaresene from dammar, dracoresene from dragon's blood, olibanoresene from olibanum.

Gluco-resins.—These are complex mixtures yielding sugars and complex resin acids on hydrolysis, as the resins of jalap and scammony.

Pharmaceutical Resins are obtained (1) by extracting the drug with alcohol and precipitating the resin in water, as with resins of jalap, scammony, ipomea and podophyllum; (2) by separating the oil from oleoresin by distillation, as rosin from turpentine and copaivic resin from copaiba; (3) by heating the plant part, as guaiac resin from guaiac wood; (4) by collecting the natural product that has exuded as oleoresin from the plant through natural or artificial punctures and from which the natural oil has partially evaporated into the atmosphere, as Burgundy pitch, mastic, sandarac, dragon's blood, etc.; (5) by collecting fossil resins, such as copal, kauri, dammar, etc.

OLEORESINS

Oleoresins are more or less homogeneous mixtures of resins and volatile oils.

There is no sharp line of demarcation between these various types of resinous substances, and classification is sometimes difficult; thus guaiac resin, which is not usually regarded as a gum-resin, may contain as much as 10 per cent of gum; small proportions of volatile oils are present in many resins, such as mastic and sandarac.

The **natural oleoresins** from the *Coniferales* include the turpentines (American, Bordeaux, Austrian, French, Venice, Strasburg), Oregon balsam, Canada balsam, Burgundy pitch, Canada pitch, spruce gum and sandarac. Those named first are liquid oleoresins, the latter ones semi-solids or solids. Usually, there is a small amount of "natural" exudation from the trees due to insect stings, broken branches, etc., but the commercial supplies are generally obtained by artificial incision through the bark and even into the wood.

GUM-RESINS

Gum-resins are mixtures consisting chiefly of resin and gum. The gum is usually a glycosidal substance similar in composition to gum acacia. Probably the only true medicinal gum-resin is gamboge, which contains no volatile oil.

Oleo-gum-resins are mixtures of resin, gum, and volatile oil and frequently small quantities of other substances. The principal medicinal oleo-gum-resins are myrrh, asafetida, galbanum, ammoniac and olibanum (frankincense).

BALSAMS

Balsams are resinous mixtures which contain large proportions of benzoic and cinnamic acids. Benzoin is sometimes referred to as a balsamic resin. The medicinal balsams include balsam of tolu, balsam of Peru, styrax (Levant and American), and benzoin (Sumatra, Siam, etc.).

VOLATILE OILS

These products are discussed very extensively in another location (see page 523), but are mentioned here especially because natural oleoresins are occasionally distilled and the volatile oil portion is separated as a valuable medicinal product. This is especially true of oil of turpentine. In other cases the coniferous leaves or twigs or fruits are steam-distilled to yield the volatile oil that is used in medicine, such as pine-needle oil, oil of juniper, oil of savin, etc.

PRODUCTS OF DESTRUCTIVE DISTILLATION

When the wood or resin of the pines is heated without access of air, a decomposition takes place and a number of volatile compounds are driven off, and charcoal remains. The condensed volatile matter usually separates into two layers: an aqueous layer containing wood naphtha (methyl alcohol) and pyroligneous (crude acetic) acid, and a tarry liquid constituting pine tar. This dry distillation is usually conducted in retorts, and if the wood be chipped or coarsely ground and the heat be applied rapidly, the yield of tar is about 10 per cent of the wood taken. The chief medicinal products are pine tar and juniper tar.

TURPENTINE

Turpentine, Gum Turpentine or Gum Thus (U. S. P. 1820 to 1916; N. F. 1916 to date) is the concrete oleoresin obtained from *Pinus palustris* Miller and from other species of *Pinus*.

"Gum" turpentine or "Gum" is a common name among the collectors and dealers, but it is a misnomer from the scientific standpoint.

Turpentine is collected in North and South Carolina, Georgia and Northern Florida. (See Fig. 40.) The trees form vast forests, and turpentine "camps," including a "still," are set up in the particular block of trees to be "worked" for the season. The larger trees are 18 to 20 inches in diameter, though trees as small as 4 or 6 inches in diameter may be "boxed." If skillfully "worked" they will yield turpentine for fifteen to twenty years. Spraying the freshly chipped faces with 40–60 per cent sulfuric acid, increases and prolongs the flow.

DESCRIPTION.—Turpentine occurs in yellowish, opaque masses, lighter internally, more or less glossy, sticky when warm, brittle in the cold. Odor and taste characteristic.

It is freely soluble in alcohol, ether, chloroform, and glacial acetic acid.

The drug constituents are volatile oil and resin. It contains not more than 2 per cent of foreign organic matter. It is employed externally in plasters as a counter-irritant.

ALLIED PRODUCTS.—*Pinus tæda*, a tall tree growing in the regions where *Pinus palustris* is found, yields an oleoresin like turpentine, though in lesser amount. *Pinus sylvestris*, or Scotch pine, which is indigenous to the mountains of Europe and Asia and extensively cultivated in this country, is the source of much of the turpentine used in Europe.

Bordeaux Turpentine is a product resembling American turpentine, and is obtained from *Pinus pinaster* and other species of *Pinus* growing in Southern France, the resin consisting chiefly, however, of the anhydride of pimaric acid.

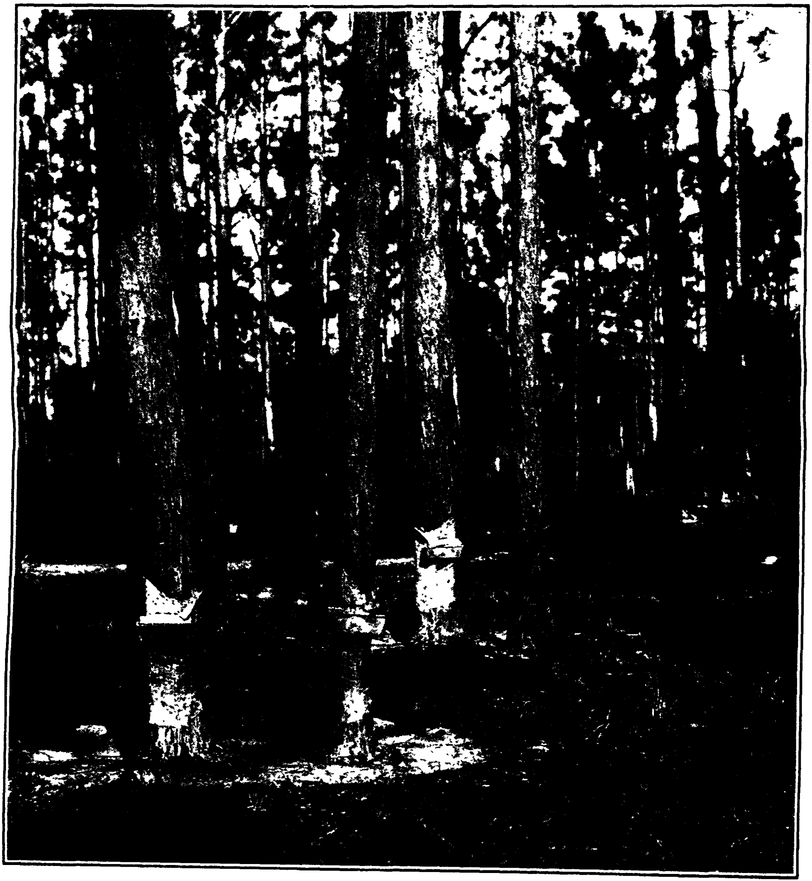


FIG. 40. Collection of turpentine. The oleoresin is secreted in the sap wood and is obtained by making triangular incisions into the bark and wood in the spring of the year; it flows into cavities ("boxes") cut lower down in the trunk, or into containers attached to the tree. The thick liquid which collects in the boxes or containers is removed into barrels and taken to the stills. The product of the first year's cutting is of superior quality and is known as "virgin" turpentine. It yields to steam distillation from 15 to 30 per cent of volatile oil, while the product of the second or third year may yield not more than 10 per cent of oil. The hot filtered residue after distillation constitutes rosin The turpentine used in medicine is the hardened "scrapings" from the trees or the containers and is largely resin. (Photo by B. V. Christensen, Gainesville, Fla.)

Venice Turpentine, or Larch Turpentine (N. F. 1916 to 1926) is an oleoresin obtained from *Larix europæa*. This larch is indigenous to the mountains of Central Europe and is extensively cultivated. Incisions are made into the heartwood in the spring and then plugged until the fall, when the viscid liquid is collected by means of a spoon. From each incision about 250 cc. is obtained annually. The oleoresin is secreted by the tree for only a few years. Commercial supplies come mostly from the Southern Tyrol.

The oleoresin is a thick, nearly clear and transparent liquid of a yellowish, yellowish green, or brown color, with a slightly green fluorescence, a characteristic aromatic odor and a slightly bitter but not acrid taste. On carefully drying a thin layer, it leaves a transparent film.

The oleoresin contains volatile oil up to 22 per cent and resin up to 80 per cent. Venice Turpentine may be adulterated with rosin or American turpentine.

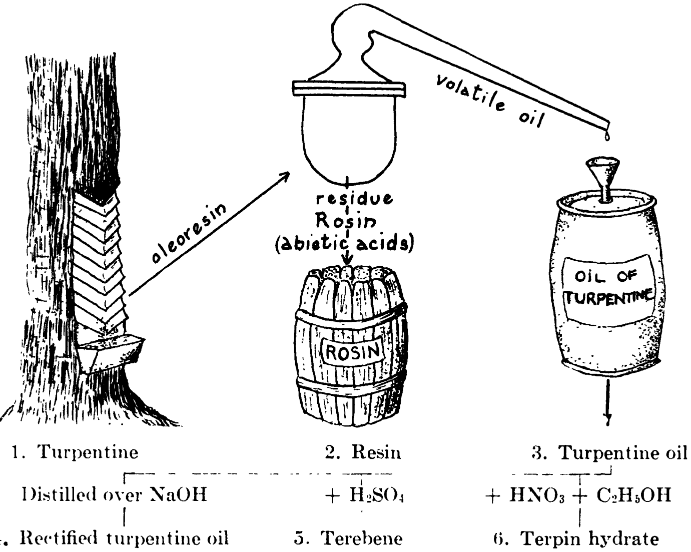


Fig. 41.—Diagrammatic scheme illustrating the relation between the official products obtained from *Pinus palustris*. (Drawing by E. H. Wirth.)

Strasburg Turpentine is the product of the European silver fir (*Abies pectinata*). It closely resembles the Canada turpentine, but has a lemon-like odor. It contains 24 to 30 per cent of a greenish, fluorescent volatile oil, consisting chiefly of *l*-pinene.

Oregon Balsam.—This is obtained from the Douglas fir (*Pseudotsuga douglasii*), a tree common in the western United States and British Columbia. The oleoresin is collected by incising the tree, and draining by means of a spout, collecting the exudation in a suitable container.

The balsam has properties and uses similar to those of Canada turpentine. For microscopic technique it is not to be recommended, as it gradually becomes granular and opaque.

Spurious mixtures have been sold under the name of "oregon balsam," and for this reason the true balsam has come to be looked upon with suspicion.

Canada Turpentine, Canada Balsam or Balsam of Fir (U. S. P. 1820 to 1916) is a liquid oleoresin, obtained from *Abies balsamea*, a tall evergreen tree indigenous to the Northern United States and Canada. The oleoresin occurs normally in reservoirs in the bark and forms in vesicles or blisters on the surface, from which it is obtained by puncturing them with the spout of the can used by the balsam collectors. It is collected chiefly in Quebec.

It is viscid, pale yellow or greenish yellow, occasionally with a greenish fluorescence, transparent, with an agreeable, terebinthinate odor, and a bitter, slightly acrid taste.

Canada balsam contains 16 to 25 per cent of volatile oil, consisting chiefly of *l*-pinene, and 70 per cent or more of resinous substances.

Canada Balsam, as a mounting medium (U. S. P. 1916 to date; N. F. 1926 to date) consists of the resin, freed from volatile oil, and dissolved in xylol to form a solution of suitable density. It is used mainly for mounting microscopic specimens and as a cement for lenses.

Burgundy Pitch (U. S. P. 1820 to 1905) is the resinous exudation of the stems of the Norway spruce fir (*Picea excelsa*), an evergreen tree indigenous to Europe and Northern Asia. The resin is obtained by making incisions through the bark into the wood, the resin exuding and solidifying; it is then collected and purified by melting it in hot water and straining the mixture.

Burgundy Pitch occurs in irregular, hard, opaque or translucent pieces, more or less plastic and strongly adhesive, yellowish brown or reddish brown; sometimes brittle, the fracture shiny and conchoidal; odor agreeable, terebinthinate; taste aromatic and sweetish.

It consists chiefly of two crystallizable resins, about 5 per cent of a volatile oil (isomeric with oil of turpentine), to which its peculiar fragrance is due; and about 10 per cent or less of water, which is included during the preparation.

Burgundy Pitch is a stimulant and counter-irritant. Formerly it was much employed in medicinal plasters.

Canada (or Hemlock) Pitch (U. S. P. 1831 to 1894) is the oleoresin of the common hemlock (*Tsuga canadensis*) and is obtained by making incisions in the trunk and collecting the exudate, or by boiling pieces of the wood and bark and skimming off the melted oleoresin. It occurs in dark, reddish brown, opaque or translucent pieces resembling Burgundy pitch, and probably contains similar constituents.

Sandarac is the dry resinous exudation of *Callitris quadrivalvis*, a large shrub of northwestern Africa. The resin exudes spontaneously, but in order to facilitate the flow and increase the yield, incisions are made.

It occurs in pale yellow, cylindrical tears, the outer surface covered with a whitish dust; fracture short, glass-like; inner surface lustrous and transparent; odor balsamic and taste slightly aromatic and bitter. It is distinguished from mastic in that it is not plastic when chewed.

Sandarac contains about 95 per cent of resin, and is used mainly in varnishes. It has been used medicinally as a mild stimulant.

A resin closely resembling sandarac is obtained from *Actinostrobus pyramidalis*, a shrub growing in southwestern Australia; and from species of *Callitris* growing in Australia and Tasmania.

Spruce Gum is a natural exudation on the branches of the black or bog spruce (*Picea mariana*), red spruce (*P. rubra*) and white spruce (*P. canadensis*). It is gathered in considerable quantities, principally in northern New England and Canada from longitudinal rifts on the branches and trunk, the finest flavor and cleanest gum from the south side of the tree.

It consists largely of a gummy substance, a small quantity of volatile oil (apparently a simple terpene), and several resins. It has medicinal properties and uses similar to gum turpentine; though rarely used medicinally, thousands of tons of spruce gum are used annually in chewing gum.

TURPENTINE OIL

Turpentine Oil, or "Spirits" of Turpentine (U. S. P. 1820 to 1947; N. F. 1947 to date) is the volatile oil distilled from the oleoresin obtained from *Pinus palustris* Miller and other species of *Pinus* which yield turpentine oils exclusively.

DESCRIPTION.—A colorless liquid having a characteristic odor and taste, both of which become stronger and more disagreeable as the oil ages or is exposed to air. It is soluble in 5 volumes of alcohol; specific gravity, 0.854 to 0.868 at 25° C.; refractive index, 1.4680 to 1.4780 at 20° C.

CONSTITUENTS.—It consists almost entirely of pinene, which in the American oil is mostly dextrorotatory, while in the European oil it is levorotatory.

USES.—It is used externally as a counter-irritant and a mild antiseptic.

Allied Products.—**Austrian turpentine oil** is derived from *Pinus nigra*, and apparently consists of dextrorotatory pinene.

French turpentine oil is derived from *Pinus pinaster*, and, while it resembles the American variety, consists entirely of lævorotatory pinene.

Rectified Turpentine Oil (U. S. P. 1894 to 1947; N. F. 1947 to date) is turpentine oil rectified by distillation from an aqueous solution of sodium hydroxide. It is to be dispensed when turpentine oil is required for internal use. It is used as an expectorant, diuretic, urinary antiseptic and anthelmintic. Average dose, 0.3 cc.

Terebene (U. S. P. 1894 to 1942) is a mixture of terpene hydrocarbons, chiefly dipentene.

Oil of turpentine is repeatedly treated with concentrated sulfuric acid until the residual "oil" is optically inactive.

Terebene is a strong stimulant to the mucous membrane and is used as an expectorant and antiseptic. Average dose: 0.25 cc.

Terpin Hydrate (U. S. P. 1894 to 1947; N. F. 1947 to date) is formed by the action of nitric acid on rectified oil of turpentine in the presence of alcohol. It is the hydrate of the dihydroxy alcohol terpin ($C_{10}H_{18}(OH)_2.H_2O$).

Terpin Hydrate is a stimulant to the mucous membrane, therefore an expectorant, diuretic and diaphoretic. Average dose, 0.25 gm.

Resin, Rosin or Colophony (U. S. P. 1820 to 1947; N. F. 1947 to date) is a solid resin obtained from *Pinus palustris* Miller and other species of *Pinus*.

The commercial grades of rosin vary in color from light amber (the finest or "water-white" grade) to almost black (and very dirty); the latter is used principally for destructive distillation and the production of "rosin oils." Rosin has a great variety of technical uses. Only the light-colored transparent rosins are used medicinally.

DESCRIPTION.—Usually in shiny, sharp, angular fragments; translucent, amber-colored, often covered with a yellowish dust; hard, brittle, easily pulverizable, fracture shallow-conchoidal; odor and taste faintly terebinthinate; soluble in alcohol, ether, benzol, carbon disulfide, acetic acid, fixed and volatile oils, and in solutions of potassium or sodium hydrate.

On heating a small quantity of rosin and neutral methyl sulfate or neutral ethyl sulfate in a test-tube, the mixture assumes a rose, then violet, and finally a deep violet color.

The alcoholic solution of rosin becomes milky-white on addition of water, and on heating fragments of rosin in water they melt, flow together and form a sticky mass.

CONSTITUENTS.—From 80 to 90 per cent of an anhydride of abietic acid, which, on treatment with alcohol, is changed into crystalline abietic acid; sylvic acid, which is probably a decomposition product of abietic acid; ash, not more than 0.1 per cent.

USES.—Rosin is used in cerates, plasters and ointments. It is slightly antiseptic and stimulant. It is employed in veterinary medicine as a diuretic. Rosin is not infrequently used as an adulterant of other resinous products, as of Burgundy pitch and Venice turpentine. A mixture of rosin and oil of turpentine is sometimes substituted for the latter.

Pine Tar (U. S. P. 1820 to date) is a product obtained by the destructive distillation of the wood of *Pinus palustris* Miller and other species of *Pinus*.

DESCRIPTION.—Semifluid, viscid, blackish brown, non-crystalline, transparent in thin layers, becoming granular or crystalline (due to the separation of pyrocatechin) and opaque with age; odor peculiar, empyreumatic, aromatic; taste pungent. Pine tar is miscible with alcohol, ether, chloroform, fixed or volatile oils, and solutions of potassium or sodium hydrate. It is heavier than water and slightly soluble in it; the solution is of a pale yellowish brown color and has an acid reaction; it yields with a dilute solution of ferric chloride, a reddish color, and with a stronger solution an olive-green color, due to the presence of pyrocatechin (distinguishing it from juniper tar); and is colored brownish red by an equal volume of calcium hydrate test solution. The petroleum ether extract is colored greenish by a 0.1 per cent solution of copper acetate.

CONSTITUENTS.—Pine tar consists of a resinous substance, with which is admixed a small quantity of turpentine, acetic acid, methyl alcohol, and various volatile empyreumatic substances. On distillation four distinct classes of products are obtained: (1) An aqueous distillate, from 10 to 20 per cent, consisting chiefly of acetic acid, methyl alcohol and acetone. (2) A light oily distillate, from 10 to 15 per cent, coming over under 150° C., and consisting of mesitylene, toluene, xylene, cumene, methene and eupion, which products are used as solvents for varnishes and similar substances. (3) A heavy oily distillate, about 15 per cent, distilling over between 150° and 250° C., and consisting of the creosote oils, viz.: phenol, cresol, creosote, paraffin, naphthalene, pyrene, chrysene, retene and some other substances. (4) A black resinous mass, called **pitch** (50 to 65 per cent) which has the odor of tar and is still official in some pharmacopœias, under the name **Pix Nigra.**

USES AND DOSE.—Pine tar is an irritant and parasiticide. It is also an expectorant. The average dose is 0.5 gm.

Oil of Tar (U. S. P. 1882 to 1916) is the volatile oil distilled from pine tar. Upon standing it becomes reddish brown in color and forms a tarry deposit.

Rectified Tar Oil (U. S. P. 1916 to 1947; N. F. 1947 to date) is the volatile oil from pine tar, rectified by steam distillation.

DESCRIPTION.—It is limpid, at first colorless, but gradually darkening to a reddish brown, and with a strong empyreumatic odor and taste, but does not form a tarry deposit. It is soluble in all proportions in alcohol. It consists largely of hydrocarbons, such as pinene, some phenol compounds, acetic and other acids.

USES AND DOSE.—It is used as an expectorant and in ointments or lotions as a parasiticide and an irritant. Average dose: 0.2 cc.

PINE OIL

Pine Oil (N. F. 1947 to date) is a volatile oil composed chiefly of tertiary and secondary terpene alcohols obtained by extraction and fractionation or by steam distillation of the wood of *Pinus palustris* Miller and other species of *Pinus*.

For either the extraction or distillation process, the wood is shredded, then fractionally steam-distilled to yield wood turpentine (coming over first) and pine oil. The dry chips are then extracted with a light petroleum distillate, which extract upon fractional distillation yields the solvent, pine oil and rosin.

DESCRIPTION.—Pine Oil is a colorless to light amber liquid with a characteristic pinaceous odor. It is easily miscible with alcohol. Specific gravity 0.925 to 0.937 at 25° C. For other constants and tests see the National Formulary.

CONSTITUENTS.—Largely a terpineol; also appreciable quantities of terpenes; secondary and tertiary alcohols; and the phenolic ether, methyl chavicol.

USES.—It is valuable in certain disinfectants and insecticides, especially in the veterinary field. It is an excellent carrier of pyrethrins and rotenone. It also has other important industrial uses; in flotation processes; in textile and paint manufacture; as a source of synthetic oils and perfumes.

Pine Oil Emulsion Concentrate (N. F. 1947 to date) is a concentrate prepared from pine oil and water using soap, sulfonated oil or other suitable emulsifying agent. It contains not less than 65 per cent, by volume, of pine oil, and not more than 10 per cent of water. It is completely miscible with 19 parts of water.

A satisfactory concentrate may be made from 74 per cent of pine oil, 8 per cent each of rosin soap and linseed soap, and 10 per cent of water. Other formulas also furnish the official concentrate.

The concentrate is a clear, colorless or pale yellow liquid, which when diluted with water (1 to 20) yields a stable emulsion. This emulsion has a phenol coefficient of 3 to 4. It is very extensively used as a disinfectant in stables, cattle cars and trucks, stock yards, etc., and as an insecticide in cattle sprays.

PINE NEEDLE OIL

Dwarf Pine Needle Oil or Pine Needle Oil (U. S. P. 1916 to 1947; N. F. 1947 to date) is the volatile oil distilled with steam from the fresh leaves of *Pinus mugo* Turra (*Pinus pumilio* Haenke). It contains not less than 3 per cent and not more than 10 per cent of esters calculated as bornyl acetate.

The Swiss mountain pine or dwarf pine is closely related to the cultivated ornamental mugho pine in the United States.

The oil is almost colorless with a pleasant, aromatic odor and a bitter, pungent taste. It is soluble in less than 10 volumes of 90 per cent alcohol, though frequently with turbidity.

The oil contains from 5 to 7 per cent of bornyl acetate; also cadinene, phellandrene, pinene and sylvestrene.

It is used as an inhalant with expectorant, stimulant and mildly antiseptic properties.

Siberian Pine Needle Oil, distilled from the leaves of *Abies siberica*, contains up to 40 per cent of bornyl esters.

Scotch Pine Needle Oil, distilled from the leaves of *Pinus sylvestris*, and German, Swedish and English Pine Needle Oils have been used medicinally.

JUNIPER

Juniper or Juniper Berries (U. S. P. 1820 to 1873; N. F. 1916 to date) is the dried fruit of *Juniperus communis* Linné and its variety *depressa* Pursh.

The generic name *Juniperus* is from the Celtic meaning rough and refers to the foliage; the specific name *communis* is from the Latin meaning, the ordinary kind. The plants are small evergreens with subulate, prickly-pointed, verticellate leaves; the fruit is a galbulus. They are indigenous to North America, Europe and Asia, the fruit being gathered in Italy, Hungary, eastern Germany and Sweden. Most of the commercial product comes from Italy. It is said that fruits from the southern climates contain larger amounts of volatile oil. Besides their pharmaceutical use, Juniper berries are employed in the manufacture of certain varieties of gin.

Description and Structure.—See Figure 42 and the National Formulary.

Powder.—Moderate brown to dark yellowish brown; odor aromatic; taste sweet, mildly terebinthinate, slightly bitter; it shows fragments composed of stone cells, the latter up to 145 microns in length; monoclinic prisms of calcium oxalate from 5 to 30 microns in length, occasionally larger; numerous fragments showing the polygonal cells of the bract epidermis, oil glands and resin masses; and of endosperm tissue.

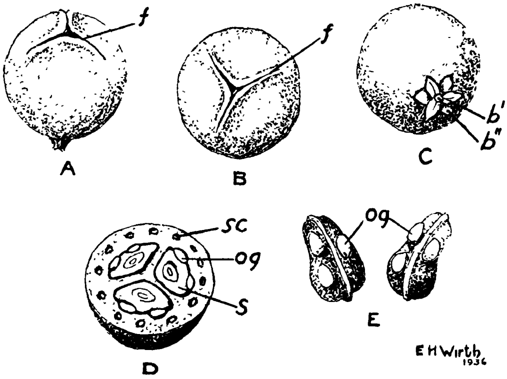


Fig. 42. *Juniperus communis.* Fruits nearly globular, about 8 mm. in diameter; externally smooth, shining, dark brown to dark purple with a blue-gray bloom. *A*, *B* and *C*, entire fruits showing the 3-rayed furrow (*f*) at the apex marking the cohesion of the three fleshy bracts and at the base two whorls of yellowish bracts, the outer whorl consisting of three narrow pointed bracts (*b'*) and the inner of three broader pointed bracts (*b"*). *D*, Transversely cut fruit showing numerous large schizogenous cavities (*sc*) in the flesh of the bract and the three triangularly ovate seeds (*s*) with large oil glands (*og*) on the surface. *E*, Seeds showing the large oil glands (*og*) on the surface. (Drawing by Wirth.)

Constituents.—Juniper contains 0.5 to 1.5 per cent of volatile oil; 10 per cent of resin; 15 to 30 per cent of dextrose; a yellow coloring principle; and yields 2 to 4 per cent of ash.

Standards.—Juniper contains not more than 10 per cent of immature or discolored fruit of the plant and not more than 3 per cent of other foreign organic matter, and yields not more than 2 per cent of acid-insoluble ash.

Uses and Dose.—Juniper is a diuretic. Average dose: 4 gm.

Juniper Oil (U. S. P. 1820 to 1947; N. F. 1947 to date) is the volatile oil distilled with steam from the dried ripe fruit of *Juniperus communis* Linné and its variety *depressa* Pursh.

This oil is a nearly colorless, limpid liquid having the characteristic odor and taste of juniper berries. It forms a neutral solution in 4 volumes of alcohol. The oil contains pinene, cadinene and juniper camphor.

USES AND DOSE.—The oil is used as a diuretic, emmenagogue and genito-urinary antiseptic. Average dose: 0.1 cc.

Juniper Tar or Oil of Cade (U. S. P. 1894 to date) is the empyreumatic volatile oil obtained from the woody portions of *Juniperus oxycedrus* Linné.

The heart wood of the shrub which is known as prickly cedar, and is indigenous to southern France and other countries bordering the Mediterranean, is cut into shavings, which are packed into tight retorts or kilns with a drain, and then heated for several hours or days. The distillate separates into an upper oily layer, which constitutes the official product, middle aqueous layer, and a lower layer of pitch.

DESCRIPTION.—A viscid, clear, dark-brown liquid, with a tar-like odor and a pungent, bitter taste. It is partially soluble in alcohol and in petroleum benzin, and completely soluble in amyl alcohol, chloroform, glacial acetic acid and in oil of turpentine. It will almost completely dissolve in 3 volumes of ether. It imparts an odor and taste and an acid reaction to water, and the aqueous solution gives a red coloration with very dilute ferric chloride solution.

CONSTITUENTS.—The sesquiterpene, cadinene, associated with some phenolic and empyreumatic compounds.

USES.—Externally as a parasiticide and a mild antiseptic.

Kien Oil, obtained in northern Europe by the destructive distillation of the wood of the root of *Pinus sylvestris,* contains *d*-pinene, *d*-sylvestrene, and, in Swedish oil, dipentene.

Lignum Juniperi, or Juniper Wood, the wood of the roots, stems and branches of *Juniperus communis,* is official in the Austrian Pharmacopœia. It occurs in commerce in pieces varying from 2 to 10 cm. in thickness with the thin bark usually adhering. The wood of the root is preferred to that of the stems and branches in that it is more aromatic. It contains a small quantity of volatile oil and resin.

The **Juniper Wood Oil** of commerce consists apparently of oil of turpentine to which some juniper oil has been added, or it is turpentine oil which has been added to juniper wood or branches and redistilled. The oil is used to some extent in veterinary medicine.

CEDAR

Savin, or Sabina (U. S. P. 1820 to 1916) consists of the tender green branches of *Juniperus sabina* Linné, an evergreen shrub indigenous to the mountainous regions of southern and central Europe and extending as far as Siberia. The young twigs are collected in the spring and dried. In the preparation of the volatile oil they are used in the green state.

The branchlets are covered, except near the base, with closely appressed scale-like leaves which are grayish or brownish green, rhomboidal, about 1 mm. long, 4-ranked, closely imbricated, thus completely covering the branchlets, and each leaf shows in cross-section a single large oil gland directly beneath the epidermis of the dorsal surface. Some of the berry-like fruits are usually present. The odor is slightly terebinthinate and the taste bitterish and resinous. The starch grains from the stems are about 4 microns in diameter; the hypodermal fibers long and up to 15 microns wide. In the powder, oleoresin masses are numerous, also fragments of narrow tracheids and of epidermis and hypodermis.

Savin contains from 4 to 6 per cent of a volatile oil, consisting of about 10 per cent of an alcohol, sabinol; 40 to 44 per cent of an ester of sabinol; pinene; cadinene; and a principle with an odor of cuminic aldehyde; also a resin and a small amount of tannin.

The drug is a diuretic. Average dose: 0.6 gm.

Savin Oil (U. S. P. 1840 to 1916) is steam distilled from the young fresh twigs of *Juniperus sabina* Linné and is similar in properties and uses to juniper oil. It has a marked stimulating effect on the uterus, hence is a powerful and dangerous emmenagogue and abortifacient.

Thuja, White Cedar or Arbor Vitæ (U. S. P. 1882 to 1894; N. F. 1916 to 1936) is the young twigs of *Thuja occidentalis* Linné, a conical tree indigenous from Quebec to Virginia, west to Minnesota and Manitoba, and extensively cultivated.

The leaves are 4-ranked and of two kinds; one opposite pair are more or less elongated, clasping, and triangular in section; the other pair is flattened, oppressed and with a prominent oleoresin gland near the middle of the under surface; the arrangement of the leaves is such as to give the branches a flattish appearance. The fruits are small cones with 6 to 10 carpels, each bearing a narrow-winged seed.

Thuja contains 1 per cent of a volatile oil with an odor resembling tansy; it contains *d*-pinene, *l*-fenchone, *d*-thujone, and an inactive oxime; the drug also contains two resins; a glycoside thujin which resembles quercitrin; a bitter glycoside pinicrin; and pinitannic acid. The two latter principles are also found in *Pinus sylvestris*.

Thuja is a stimulant, a diuretic, an emmenagogue and an irritant. The average dose of the drug is 2 gm.

Cedar Leaf Oil, Oil of Thuja or Oil of Arbor Vitæ (U. S. P. 1942 to date) is the volatile oil distilled with steam from the fresh leaves of *Thuja occidentalis* Linné.

Description.—Cedar Leaf Oil is a colorless or yellow liquid with a characteristic, pleasantly aromatic odor; specific gravity 0.910 to 0.920; soluble in three volumes of 70 per cent alcohol. It contains not less than 60 per cent of ketones, calculated as thujone. For other constants and assay process see the U. S. Pharmacopœia.

Constituents.—Cedar Leaf Oil contains *l*-fenchone, *d*-thujone and *a*-pinene, the first two giving the pharmacologic effects to the oil.

Uses and Dose.—The oil is stimulant to heart and uterine muscle; in overdose, abortifacient and convulsant. It has been used as a stimulant, an irritant and an antiseptic. It entered the U. S. Pharmacopœia as an aromatic substitute for lavender oil in soap liniment, because of the war shortage of lavender oil. Average dose: 200 mg.

Red Cedar (U. S. P. 1820 to 1894) consists of the young leafy twigs of *Juniperus virginiana* Linné. This tree or shrub is of wide distribution in North America. The fruits are purple, smaller, and contain fewer seeds than those of *Juniperus sabina*. The constituents also are similar. The volatile oil of the wood is known as cedarwood oil and occurs to the extent of 2.5 to 4.5 per cent. The oil consists of cedrol, or so-called cedar camphor, and cedrene.

Cedar Oil or Cedarwood Oil (U. S. P. 1916 to date) is a selected commercial oil distilled from the wood of red cedar, *Juniperus virginiana* Linné, with a refractive index of about 1.504 at 20° C., to be used for "clearing" sections of plant or animal tissue for viewing under the microscope.

Immersion Oil is cedar oil especially prepared to have a refractive index of exactly 1.515 at 18° C., for use with homogeneous immersion lenses.

PINACEOUS BARKS

White Pine (N. F. 1916 to date) is the dried inner bark of *Pinus strobus* Linné. The White or Weymouth Pine is the principal timber pine of the northern United States and Canada. The outer corky layer of the bark is removed before the inner portion is dried.

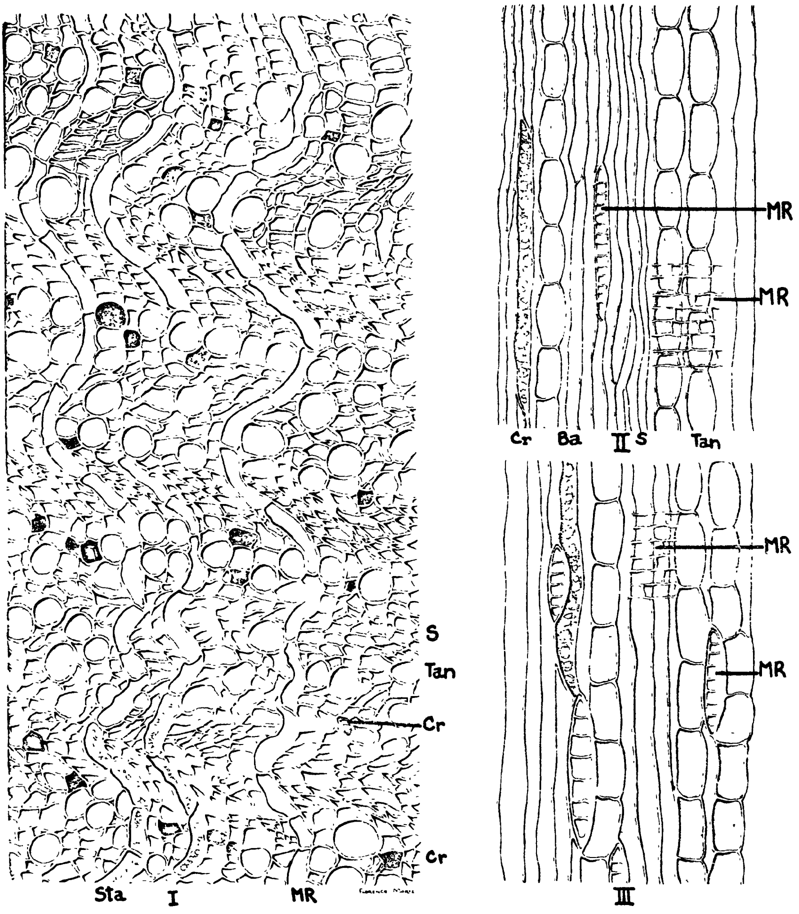


FIG. 43.—White pine bark: *I*, Transverse section; *II*, radial-longitudinal section; *III*, tangential-longitudinal section. *MR*, Very wavy medullary rays as noted in the transverse view, and which causes the appearance of the rays in the radial and tangential-longitudinal views to be nearly alike; *Cr*, prisms of calcium oxalate embedded in brown, insoluble, resin-like material contained in elongated fiber-like cells; *Ba*, narrow, elongated fiber-like cells with unthickened non-lignified walls; *S*, sieve with more or less collapsed, narrow, elongated cells; *Sta*, starch; *Tan*, large, longitudinally elongated tannin cells. (Drawing by Martz.)

Pinus is the ancient Latin name, probably akin to *pinna*, meaning a feather, and has reference to a somewhat feather-like foliage of many of the species. The specific name *strobus* pertains to the cones or strobiles.

Description, Histology and Powder.—See Figure 43 and the National Formulary.

Constituents.—The alcoholic extract forms about 30 per cent of the drug and contains tannic acid and an oleoresin; the bark contains considerable mucilage and a small quantity of coniferin; the latter is usually present in the cambial layer of all of the species of *Pinus* as well as in other genera of the *Pinaceæ*. Total ash is not more than 2 per cent and adhering outer bark not more than 1.5 per cent of the drug.

Larch Bark is the inner bark of the branches and trunk of *Larix decidua*. It occurs in quills and flattened, more or less transversely curved pieces, outer surface light to dark red; inner surface yellowish white to pinkish red; fracture short-fibrous; odor aromatic; taste astringent and somewhat bitter. The bark contains scattered groups of stone cells with thick lamellated walls, the cells varying in shape from branching to long spindle-shaped forms resembling bast fibers. Larch bark contains 10 to 15 per cent of tannin, a small quantity of volatile oil, resin and larixinic acid. The latter sublimes at 93° C., forming crystals resembling those of benzoic acid. It is allied to pyrogallol and pyrocatechin and occurs mostly in the bark of young trees.

Hemlock Bark from *Tsuga canadensis*, is very extensively used in the United States for tanning. The inner bark is used to some extent in medicine as an astringent. The drug comes in flattened pieces, varying in size; the outer surface is cinnamon-brown or blackish brown and longitudinally wrinkled, or evenly furrowed; inner surface yellowish brown to cinnamon-brown, finely striate and with numerous small crystals; fracture short in the outer portion and strongly fibrous in the inner bark; the odor is faint and the taste strongly astringent. It contains from 10 to 15 per cent of tannin and a small quantity of volatile oil and resin.

GNETALES

This order contains but one family, the *Gnetaceæ*, a small family of three genera and about forty species, of great interest to botanists, since it connects the Gymnosperms with the Angiosperms. Several species of *Gnetum* yield edible fruits and gums. Medicinally the genus *Ephedra* is of the greatest interest. At least three groups of *Ephedra* species have been studied for their active constituents: (*a*) the Asiatic group consisting of *E. sinica*, *E. equisetina* and other species; (*b*) the European group, *E. vulgaris* variety *helvetica;* (*c*) the American group, six or more species found in southern California and Mexico. Probably none of our American species contains an alkaloid, but the Chinese plant, *E. sinica*, contains the alkaloid ephedrine.

EPHEDRA

Ephedra or Ma-Huang is the entire plant, or the overground portion of *Ephedra sinica* grown in China. In Chinese characters "Ma" means astringent and "Huang" means yellow, probably referring to the taste and color of the drug. It has been used as a medicine in China for more than five thousand years. Its use in modern medicine began with the recent discovery of the valuable properties of ephedrine. The plant is found near the sea coast in southern China and the drug is exported from Canton.

The plant is a low, diœcious, practically leafless shrub, 60 to 90 cm. high. The stem, green in color, is slender, erect, small ribbed and channeled, 1.5 mm. in diameter and usually terminating in a sharp point. Nodes are 4 to 6 cm. apart, at which the leaves appear as whitish triangular scarious sheaths. Small blossoms appear in the summer.

For the structure see Figure 44.

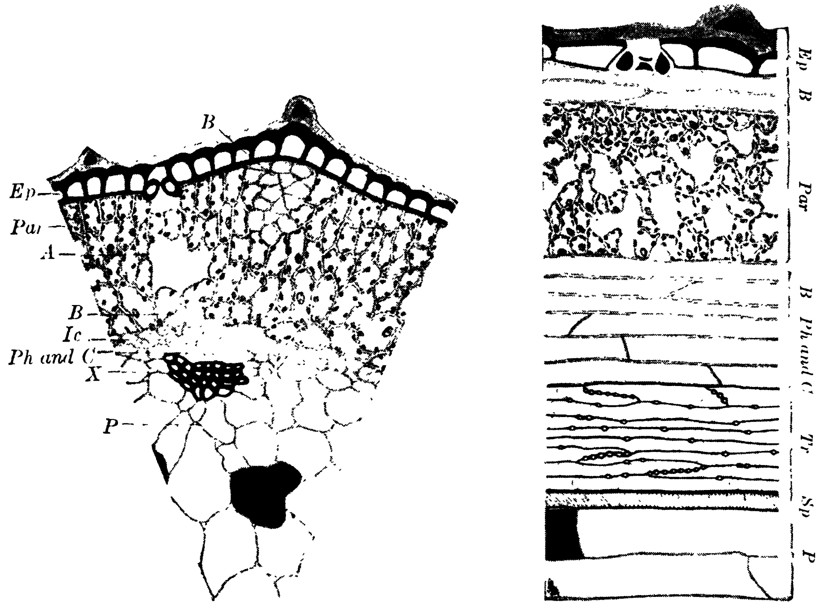


FIG. 44.—Transverse section of the stem of Ma Huang. *Ep*, Epidermis with heavily cutinized outer wall, depressed stoma and an occasional cell with a slight projection forming a rib; cortex of thin-walled, spongy chlorenchyma (*Par*), an occasional air space (*A*), and a bundle of bast fibers (*B*), beneath a rib or associated with each of the small, open-collateral vascular bundles which contain a primary xylem (*X*) of spiral and dotted tracheal tubes and a secondary xylem of tracheids with bordered pits; *Ph and C*, phloem and fascicular cambium; *Ic*, interfascicular cambium with starch granules; *P*, pith. (After K. K. Chen.)

Ephedrine (U. S. P. 1936 to date) is an alkaloid obtained from *Ephedra equisetina* Bunge, *Ephedra sinica* Stapf and other species of *Ephedra*, or produced synthetically.

DESCRIPTION.—Ephedrine occurs in white, rosette or needle crystals, or as an unctuous mass. It is soluble in water, alcohol, chloroform, ether and in liquid petrolatum, the latter solution being turbid if the ephedrine is not dry.

TESTS.—Ephedrine melts between 34° and 40° C., depending upon the amount of water it contains; it contains not more than 0.1 per cent of ash; its solutions are alkaline to litmus; it readily forms salts with acids; and responds to the usual tests for alkaloids. For other tests see the U. S. Pharmacopœia.

USES AND DOSE.—Ephedrine excites the sympathetic nervous system, depressing smooth and cardiac muscle action and produces effects similar to those of epinephrine. It produces a rather lasting rise of blood-pressure and mydriasis and diminishes hyperemia. The alkaloid may be used in 0.5 to 2 per cent oil spray.

Ephedrine Hydrochloride (U. S. P. 1936 to date) $C_{10}H_{15}ON.HCl$, when dried over sulfuric acid for twenty-four hours, contains not less than 80 per cent and not more than 82.5 per cent of anhydrous ephedrine, $C_{10}H_{15}ON$.

Ephedrine Sulfate (U. S. P. 1936 to date), $(C_{10}H_{15}ON)_2.H_2SO_4$, when dried over sulfuric acid for twenty-four hours contains not less than 75.5 per cent and not more than 77.3 per cent of anhydrous ephedrine $C_{10}H_{15}ON$.

Both of these salts are readily soluble in water and in hot alcohol, but not in ether. They have the same pharmacological properties as ephedrine and are used orally in an average dose of 0.25 gm. They are also used, in aqueous solution, intramuscularly and intravenously.

ANGIOSPERMÆ OR ANGIOSPERMS

The Angiosperms are represented by at least 130,000 living species as compared with 650 species of Gymnosperms and 5000 species or less of Pteridophytes including the ferns.

The Angiosperms form the most recent development of plants. They did not occur in the Paleozoic age and but to a slight extent in the Mesozoic. They are adapted to the land better than other great plant groups and are found in every part of the world where plants can live. They are distinguished from Gymnosperms by the following features: The stamens and pistils (carpels) are borne, frequently together, in flowers; the ovules are found in closed ovaries, the pollen is received on the stigma and the pollen nuclei are conveyed by means of pollen tubes to the ovule; tracheal tubes usually occur both in the primary and secondary xylem; many herbaceous annual or biennial forms occur, whereas Gymnosperms are all woody perennials.

MONOCOTYLEDONEÆ OR MONOCOTYLEDONS

This class of Angiosperms includes those plants in which the seed contains but one cotyledon. The stems are endogenous and contain concentric or closed collateral fibrovascular bundles. The leaves are usually parallel-veined and in the majority of cases have entire margins. The flowers are mostly trimerous.

GRAMINEÆ, OR GRASS FAMILY

These are mostly herbs with cylindrical, usually hollow stems (culms) closed at the swollen nodes. The leaves are alternate, the basal portion or sheath enveloping the culm and bearing at the orifice an appendage called the ligule. Under the epidermis of both stems and leaves there is a more or less strongly developed ring of sclerenchymatous fibers; similar fibers surround the fibrovascular bundles which occur in one or more circles beneath the endodermis when present.

The flowers are mostly hermaphroditic and are borne on spikelets. The axis of the spikelet is called a rachilla. The lowest pair of bracts on the spikelet are called glumes and bear no flowers. The higher bracts each support a flower and are called lemmæ, palæ or flowering glumes. The fruit is a caryopsis. The family is of vast economic use, supplying the world with cereal grains, forage crops and other valuable products.

STARCHES

Probably no other single organic compound is so widely distributed in plants as is **starch**. It is produced in large quantities in green leaves as the temporary storage form of photosynthetic products. As a permanent reserve food material for the plant, it occurs in seeds and in the pith, medullary rays and cortex of the stems and roots of perennials, etc. It constitutes from 50 to 65 per cent of the dry weight of cereal seeds and as high as 80 per cent of the dry matter of potato tubers.

In the United States alone, not less than 850,000,000 pounds of pure starch are marketed annually; of this amount almost five-sixths is made from Indian corn. While starch is widely distributed in the plant kingdom, there are relatively few plants from which it is obtained on

THE CHARACTERISTICS OF FIFTEEN RATHER COMMON STARCHES ARE

Starch	Botanical Source	Occurrence in cell	Shape*
Indian corn	*Zea mays*	Simple; may be united, but not in true aggregates	Polygonal or irregularly ovoid
Rice	*Oryza sativa*	Mostly round or oval aggregates of up to 100 grains	Polygonal or somewhat rounded
Wheat	*Triticum æstivum*	Large grains never united; small grains rarely	Large grains lenticular, small grains globular
Rye	*Secale cereale*	Similar to wheat	Similar to wheat
Barley	*Hordeum vulgare*	Similar to wheat	Similar to wheat, occasionally ovoid
Oat	*Avena sativa*	Mostly round or oval aggregates of many grains	Rounded, polygonal and spindle-shaped forms
Buckwheat	*Fagopyrum sagittatum*	A few rod-shaped aggregates	Polygonal or rounded polygonal
Potato	*Solanum tuberosum*	Aggregates rare	Ovoid, pyriform, ellipsoidal (oyster-shell forms)
Bermuda arrowroot	*Maranta arundinacea*	Aggregates rare or absent	Ovoid, pyriform, spindle-shaped
Kidney bean	*Phaseolus vulgaris*	Aggregates rare	Reniform, ovoid, ellipsoidal
Pea	*Pisum sativum*	Aggregates rare	Ellipsoidal, ovoid, subreniform
Cassava	*Manihot esculenta*	Numerous aggregates of 2 to 8 grains	"Kettle-drum" and "sugar loaf" shape; truncate
Sago	*Metroxylon* sp. *Cycas* sp.	Some aggregates of 2 to 5 grains	Ovoid, irregular, plano-convex
Edible canna	*Canna edulis*	Aggregates rare	Broadly ellipsoidal, flattened, beaked
Sweet potato	*Ipomæa batatas*	Aggregates of 2 to 6 grains	Plano-convex; bell-shaped forms

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* This applies to the simple grains and the components of the aggregates.

a large scale. In addition to corn, other cereals, as rice and wheat, contribute to the world's supply. Commercial starch is also obtained from potato tubers, maranta rhizomes and cassava roots.

Starch occurs in granules (or grains) having characteristic striations. These striations and the size and shape of the granules are more or less characteristic in many species of plants and may be used as a microscopic means for identifying the botanical origin of the starch. In this manner

CLASSIFIED IN THE FOLLOWING TABLE (ALSO SEE FIGS. 45 AND 46)

Size in microns*	Hilum*	Striations*	Polarization*
10–35, mostly 20–30	Central; radiating clefts	Invisible	Distinct
2–10, mostly 3–7	Central, indistinct	Invisible	Distinct
Large 28–35, small 2–10	Central; dot; clefts rare	Indistinct	Indistinct
Large 25–60, small 3–10	Central; dot; occasional 3- or 4-rayed clefts	Concentric	Distinct
Large 18–30, small 2–10	Central; dot; occasional 3- or 4-rayed clefts	Concentric; indistinct	Distinct
Simple 2–12, mostly 5–10	Invisible	Invisible	
2–15, mostly 6–12	Central, conspicuous	Invisible	Distinct
2–115, mostly 45–70	Circular; at small end of grain	Distinct; eccentric	Very distinct
10–75, mostly 40–65	"Flying bird" hilum in broad end	Distinct; eccentric	Very distinct
25–60, mostly 30–45	Central; elongated branching cleft	Distinct; concentric	Distinct
15–55, mostly 20–45	Central; like bean, but less cleft	Distinct; concentric	Distinct; similar to bean starch
4–35, mostly 15–25	Central; distinct; often triangular; occasional clefts	Indistinct	Distinct
10–80, mostly 30–50	Eccentric; usually cleft	Concentric and eccentric	Distinct
18–135, mostly 50–100	Eccentric; dot near narrow end	Concentric and eccentric	Distinct
2–55, mostly 25–35	Distinct; usually slightly eccentric; occasional clefts	Indistinct	Distinct

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* This applies to the simple grains and the components of the aggregates.

the identity of many food and drug products, of vegetable origin may be established.

General Properties of Starch.—The starches are substances of high molecular weight, whose constitution is represented by the general formula $(C_6H_{10}O_5)n$. The value of n has not been accurately determined for any of the individual members of the group but is probably somewhere in the neighborhood of 1500.

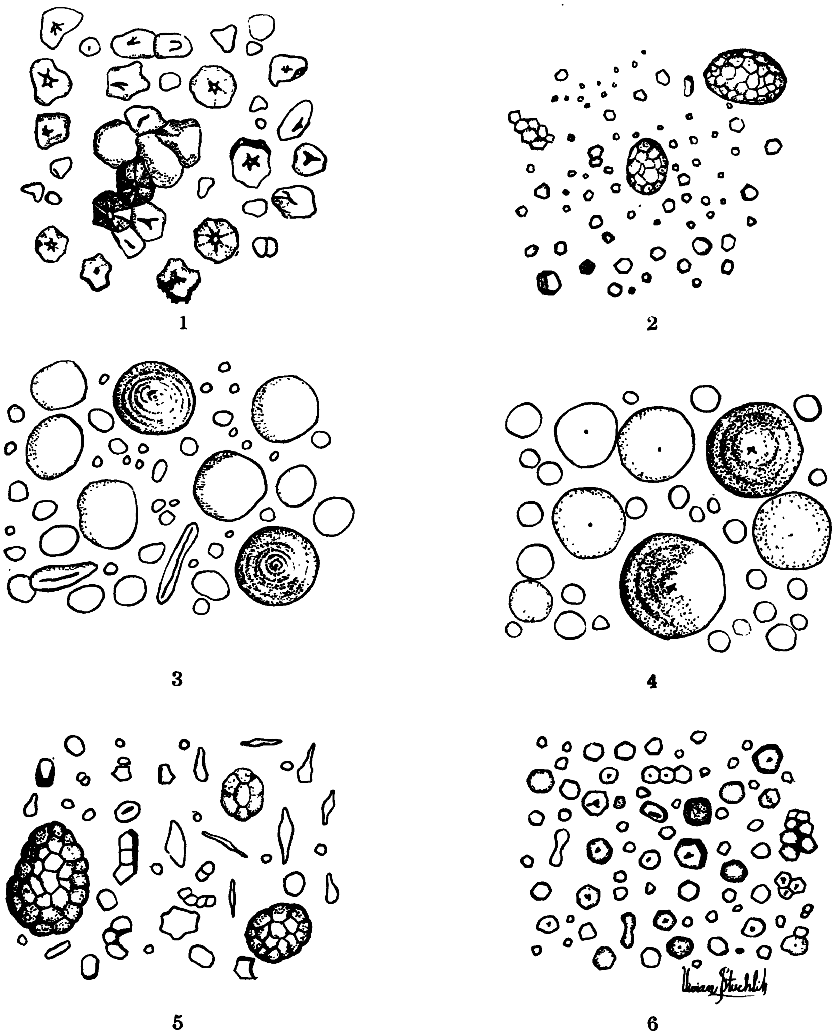


Fig. 45.—Starches: 1, Corn starch; 2, rice starch; 3, wheat starch; 4, rye starch; 5, oat starch; 6, buckwheat starch. (Drawings by Vivian J. Stuchlik.)

Starches generally form colloidal sols rather than true solutions. If a suspension of starch in cold water be added, with stirring, to boiling water, the opaque granules swell and finally rupture to give a translucent sol. If this is somewhat concentrated, it will set to a firm jelly on cooling. Cold concentrated aqueous solutions of the caustic alkalis, of chloral hydrate, of ammonium thiocyanate, or of hydrochloric acid also cause the swelling and ultimate rupture of the starch granules to form pastes.

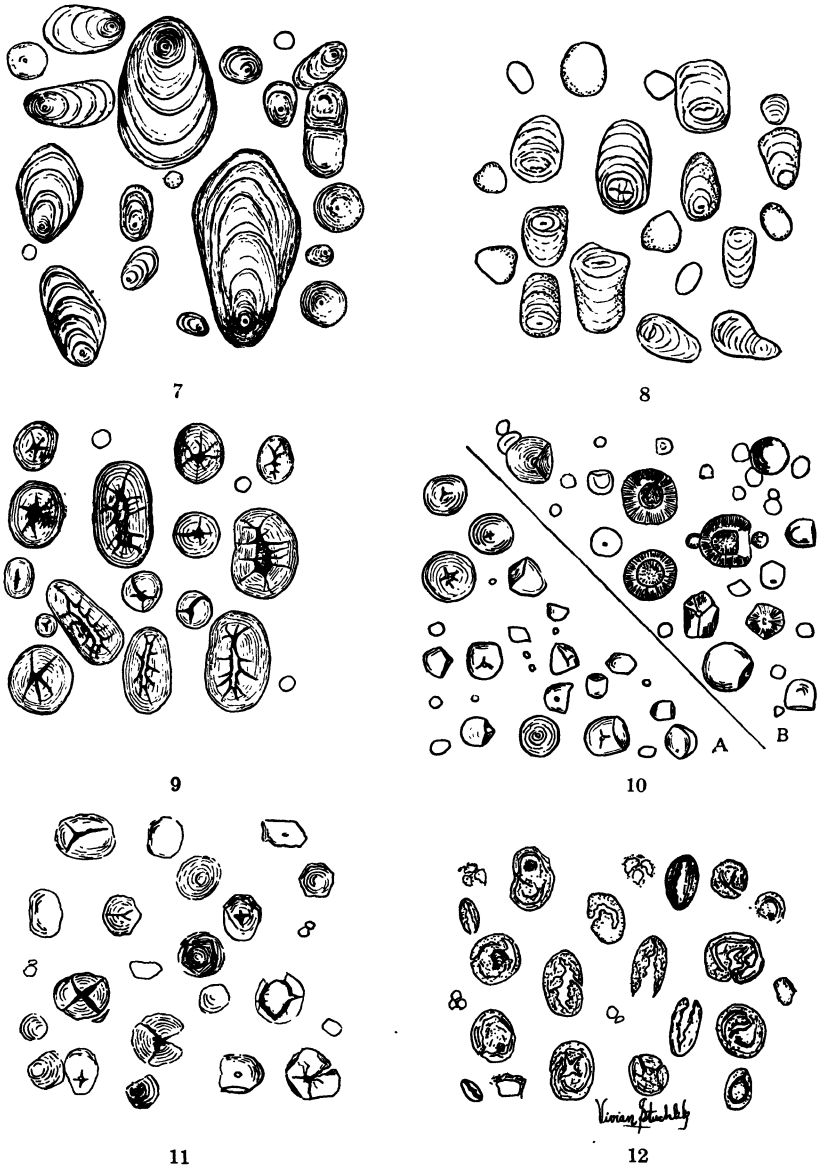


FIG. 46.—Starches: 7, potato starch; 8, Bermuda arrowroot starch; 9, bean starch; 10*A*, cassava starch; 10*B*, tapioca starch (cassava starch altered by heat); 11, yellow dextrin (corn starch altered by treatment with heat); 12, malt (barley starch altered by diastase). (Drawings by Vivian J. Stuchlik.)

It is claimed that when starch is heated in the presence of water, two product, are formed: α-amylose (starch cellulose, amylopectin, amylocellulose), insoluble in water and forming the slimy portion of the paste; and β-amylose (granulose or amylose) which is water soluble. These have been separated, to some extents by sedimentation, centrifugation, selective destruction of one component by enzymatic action, or by other means. β-Amylose gives the characteristic blue color with iodine; α-amylose, a bluish red or plum color. Others claim that the starch granules are quite uniform throughout and that the distinction between α- and β-amylose is due to the fact that the outer layers of the granule are more dehydrated and more resistant to chemical action.

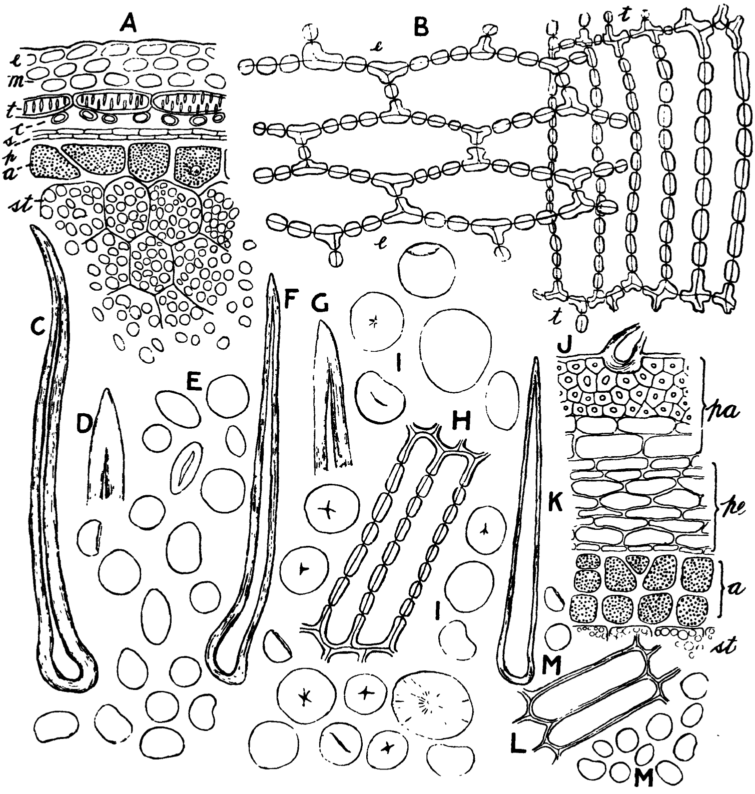


FIG. 47.—**Wheat** grain (*Triticum æstivum*): *A*, Transverse section showing epicarp (*e*), cells of mesocarp (*m*), tangentially elongated cells (*t*), tube cells (*c*), spermoderm (*s*), perisperm (*p*), aleurone cells (*a*), parenchyma containing starch (*st*); *B*, surface section of pericarp showing relation of epidermal cells (*e*) to tangentially elongated cells (*t*); *C*, hair from the summit of the grain with thick wall and very narrow lumen; *D*, apical portion of a hair; *E*, starch grains. **Rye** grain (*Secale cereale*): *F*, hair with wall comparatively thinner than in the hair of the wheat grain; *G*, apical portion of a hair; *H*, tangentially elongated cells in which the pores occur only on the tangential walls; *I*, starch grains which vary from 0.020 to 0.070 mm. in diameter, and occasionally have delicate clefts. **Barley** grain (*Hordeum vulgare*): *J*, transverse section of palet (*pa*) and pericarp (*pe*), aleurone layer (*a*) composed of two or three rows of cells, parenchyma of endosperm containing starch (*st*); *K*, hair from epicarp with very thin wall and large lumen; *L*, tangentially elongated cells which differ from those of wheat and rye in being without pores; *M*, starch grains which resemble those of wheat but are uniformly smaller.

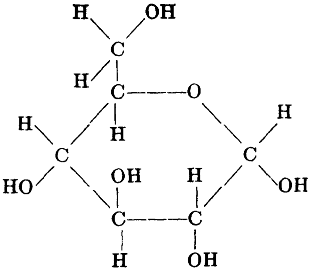
Amylases, such as diastase, hydrolyze starch to dextrins and these in turn to maltose which is the end product of diastatic action. Acids or maltase continue the hydrolysis to glucose. The various hydrolytic products have been given names and it has been suggested that the following scheme represents the progress of hydrolysis:

Starch → Amylodextrin → Erythrodextrin + Maltose
↓
Achroodextrin + Maltose
↓
Maltose
↓
Glucose

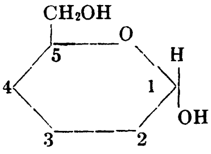
These changes can be traced by the iodine color reaction: starch will show its characteristic blue; dextrins purple, red or red-brown; and glucose gives no color with iodine. It has been suggested that these color changes may mean nothing more than a change in the *size* of the starch particle, the diastase only dispersing the starch molecules and not forming distinct compounds, the color reactions with iodine being colloidal phenomena depending upon the degree of dispersion.

When dry starch is heated at about 50° C. for from fifteen to thirty minutes, the lamellæ and crystalloidal structure become better defined and the polarizing effects produced by the grains also become more pronounced. When starch is mounted in a fixed oil, as almond, the polarizing effects are more pronounced than when it is mounted in water, but the inner structure is not usually apparent, unless the starch has been previously heated.

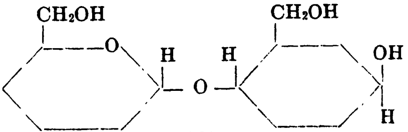
Chemistry of Starch.—If we assume glucose to exist in the pyranose form (I) we may then simplify the expression of its formula as illustrated in (II) and maltose may be expressed by formula III.



I

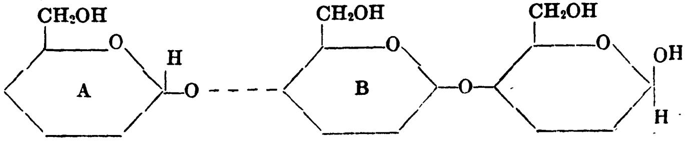


II



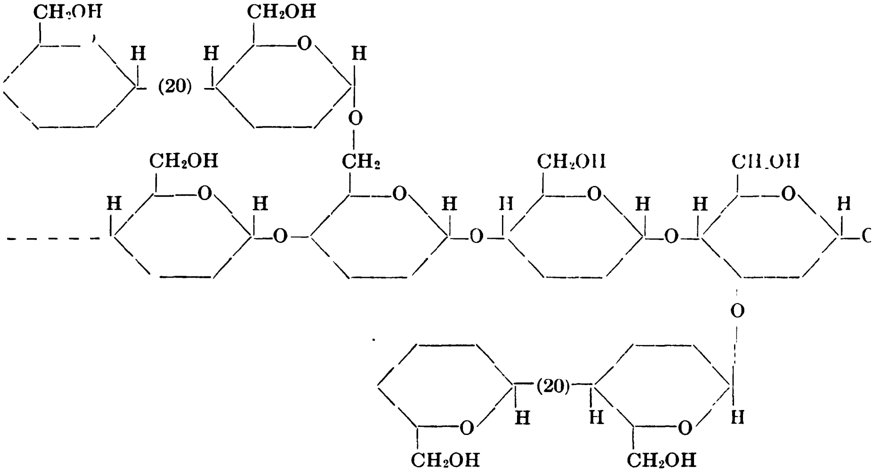
III

Applying methylation processes to maltose Haworth obtained both 2,3,6-trimethylglucose and 2,3,4,6-tetramethylglucose. Extending the technique to starch he obtained besides 2,3,6-trimethylglucose, about 4.5 per cent of 2,3,4,6-tetramethylglucose and suggested the following chain structure for starch (IV).



IV

For every twenty to twenty-five glucopyranose units present in the chain (B) yielding 2,3,6-trimethylglucose there is one unit (A) present yielding 2,3,4,6-tetramethylglucose. Richardson suggested that some 1000 units comprised the chain. Staudinger demonstrated that starch was in reality composed of extremely large molecules (about 1500 glucopyranose units) and not simply aggregates of molecules. These large molecules appeared to be highly convoluted and Staudinger proposed the symmetrically branched configuration for starch shown in (V).



V

According to available data starch appears to be a mixture of molecules. Corn starch, for example is composed of about 70 per cent of IV and about 30 per cent of V. Corn starch obtained from waxy maise, however, consists almost entirely of the type indicated in V.

Dextrin is a mixture of soluble carbohydrates, such as amylodextrin, achroodextrin and maltodextrin, together with a variable quantity of unconverted starch. It is prepared by partially hydrolyzing starch (see page 133). When dry starch is heated with steam at 180° to 200° C., **yellow dextrin** or **British gum** results

White Dextrin (N. F. 1916 to 1936; in culture media, N. F. 1936 to date) is formed from starch moistened with a very dilute mineral acid and heated to 110° C. The dextrins are chiefly prepared from corn starch in the United States and potato starch in Europe. Dextrin should be completely soluble in hot water and should not contain more than 5 per cent of dextrose (portion soluble in boiling alcohol), 10 per cent of moisture and 0.5 per cent of ash. Dextrin is used as an adhesive, for sizing cloth or paper, in calico printing, etc.

Flour is the sifted, finely ground grain of wheat, rye, barley, rice, buckwheat, etc. Flours consist largely of starch but also contain small fragments of tissues of the embryo, endosperm, and other parts of the grain.

Gluten (U. S. P. 1936 to date, in a vitamin assay) is a protein which becomes sticky when mixed with water; it is found in rye flour and more abundantly in wheat flour. The property of forming a dough is due to the gluten that flours contain.

Particles of the grains which cannot be milled fine enough to pass through the bolting cloths are separated and form what is commercially known as

bran, middlings or **shorts.** In commercial milling usually the grains are first coarsely crushed, thus permitting the separation of the coarser particles of the pericarp and seed coat, which form the **bran.**

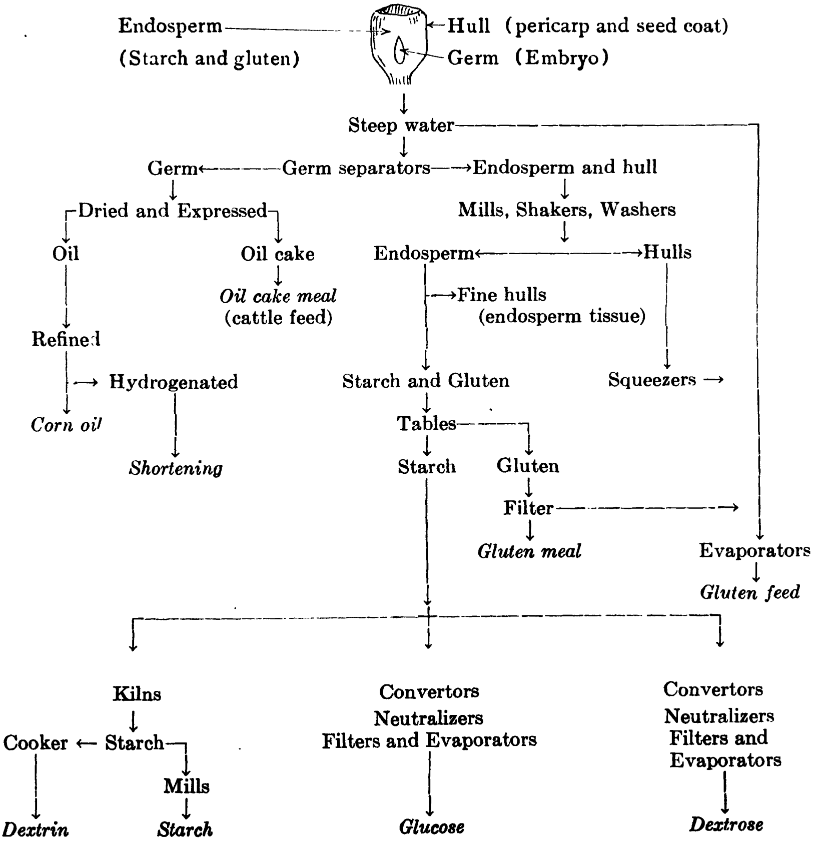
The flour is sifted out after each subsequent crushing until finally only fragments of tissue remain, together with some adhering starch and gluten, which constitutes **middlings.** The **germ** (embryo) is usually first removed from the grain before making flour, as it contains considerable fat which readily becomes rancid and injures the quality of the flour. The germ is used to some extent as a food and yields an oil (wheat oil, corn oil), which is the source of **Vitamin E.**

Flours may be distinguished from starches microscopically by the presence of hairs and other tissue of the grain (see Fig. 47). Wheat flour, when moistened with water, forms a sticky mass; while wheat starch, similarly moistened, forms a simple suspension having no mucilaginous properties.

If corn or any cereal grain is coarsely ground, the resulting product is known as **meal** or **grits.** These may be identified by the characters of their starch grains as well as by the presence of characteristic hairs and other pericarp tissue.

Other Varieties of Zea Mays.—Among other varieties of *Zea mays* commonly occurring in commerce may be mentioned *Zea mays everta* to which belong the pop-corns; *Zea mays indentata*, the dent corns; *Zea mays indurata*, the flint corns; and *Zea mays saccharata*, the sweet or sugar corns.

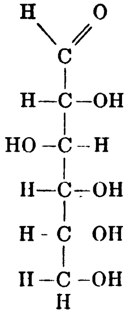
GRAIN OF CORN

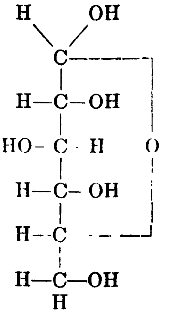


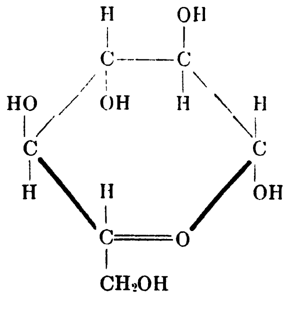
SUGARS

Sugars are simple carbohydrates and since they possess a characteristic sweet taste the term saccharide has been employed as a basis for the classification of this entire carbohydrate group. The monosaccharides include the hexoses, which are simple sugars having the formula $C_6H_{12}O_6$. The disaccharides, which may be regarded as being derived from the combination of two molecules of hexose with the dropping out of one molecule of water, have the formula $C_{12}H_{22}O_{11}$. The trisaccharides have the formula $C_{18}H_{32}O_{16}$.

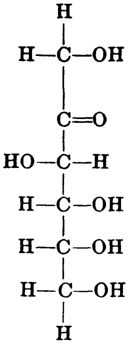
Monosaccharides.—Chemically speaking, the definition of a simple sugar is a substance belonging to the carbohydrate group which is a ketonic or aldehydic substitution product of a polyhydric alcohol. The simplest of these would be a diose H.(CHOH).CHO, which although it does not occur in nature, probably enters into many plant syntheses. An aldehydic and a ketonic triose are possible (glyceric aldehyde and dihydroxy acetone), but do not occur free in nature, although certain organisms are capable of oxidizing glycerin to dihydroxy acetone. The tetroses also have not been found in nature. Pentoses however, occur commonly in nature usually as products of hydrolysis of hemicelluloses, gums and mucilages. Hexoses are by far the most important monosaccharides found in plants. They are the first detectable sugars synthesized by plants and form the units from which most of the polysaccharides are constructed. There are 16 possible aldohexoses and 8 ketohexoses, of which, if we consider both the alpha and beta forms, permits 48 isomers. Of these, only 2 are found occurring in the free state in plants. They are levulose (fructose) and dextrose (glucose). Both are found in sweet fruits, honey and invert sugar. When starch is completely hydrolyzed it yields *d*-glucose, while inulin yields fructose upon hydrolysis. *Glucose* is an aldohexose, that is, a polyhydric alcohol having an aldehydic group while *fructose* having a ketone group is a ketohexose. These groups explain the reducing properties of the monosaccharides and account for the commonly applied term "reducing sugars." The hexoses may be considered as six-membered open chain compounds, five of the carbon atoms each having an attached alcohol group and the sixth the aldehyde or ketone group. Such an aliphatic formula readily illustrates and explains stereoisomerism, but many of the other properties of the hexoses can only be explained on the basis of a ring structure. Thus glucose possesses an amylene-oxide ring. The following formulas have been assigned to glucose:

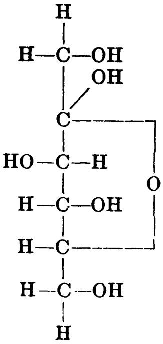


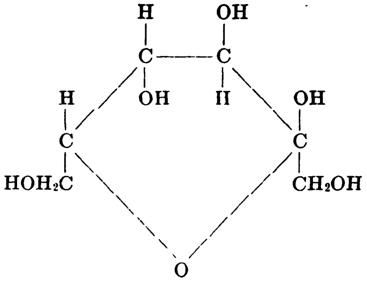




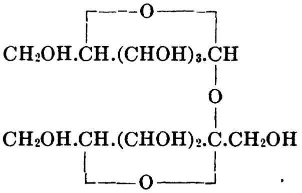
Fructose on the other hand may be represented as a straight-chain compound or as a butylene-oxide ring. The following formulas have been assigned to it:





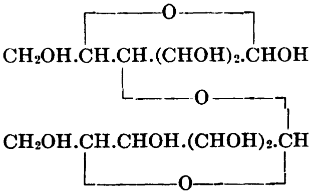


Disaccharides.—Of the disaccharides, sucrose is the only member found occurring in the free state in plants, although maltose has been reported as occasionally present in the cell sap. Sucrose occurs in fruit juices, sugar cane, sugar beet, the sap of certain maples and in many other plants. Upon hydrolysis it yields **invert sugar** which consists of molecularly equal quantities of dextrose and levulose. Sucrose is a non-reducing sugar and may be expressed by the following formula:



$$\begin{array}{c} CH_2OH.CH.(CHOH)_3.CH \\ O \\ CH_2OH.CH.(CHOH)_2.C.CH_2OH \end{array}$$

Maltose, while seldom occurring in the free state in Nature, is produced in large quantities by the hydrolysis of starch during the germination of barley and other grains (diastatic fermentation). It is a reducing sugar and upon hydrolysis yields two molecules of dextrose. Maltose may be expressed by the following formula:



$$\begin{array}{c} CH_2OH.CH.CH.(CHOH)_2.CHOH \\ O \\ CH_2OH.CH.CHOH.(CHOH)_2.CH \end{array}$$

The four sugars mentioned (dextrose, levulose, sucrose and maltose) are those most commonly occurring in vegetable drugs. Certain other sugars, however, occur to a limited extent in Nature, either in the free state or in glycosidal combination. Among these are the monosaccharides, mannose (occurring in mannosans) and galactose (a constituent of lactose and raffinose), and the disaccharides trehalose (which is found widely distributed in the fungi) and lactose (milk sugar). Maltose and lactose possess functional aldehyde groups and so are reducing sugars. Sucrose and trehalose are non-reducing sugars.

Microchemistry of the Sugars.—Although sugars are easily soluble in water and occur in solution in the living cell, it is very seldom that they crystallize upon the drying of plant material. If the dry plant material be extracted with water the sugar will dissolve and may be identified by certain microchemical reactions, among which the following are useful:

The Molisch Reaction.—Mix about 5 drops of the aqueous extract with 2 drops of a 15 per cent solution of α-naphthol in alcohol, preferably in a small white porcelain evaporating dish or on a spot-plate. Add an equal volume of concentrated sulfuric acid and agitate. The presence of sugar is indicated by a deep violet color. Dilution with water will cause the separation of a bluish violet precipitate which is soluble in ether or alcohol with a yellow color; in potassium hydroxide T.S. with a yellow color; and in ammonia, yellowish brown droplets are formed.

The reaction is not specific for sugars, as other carbohydrates (inulin, starch, cellulose, etc.) and glucosides will also react positively. It is probable that the sulfuric acid splits off sugar from the more complex carbohydrates, which sugar in turn gives the color reaction.

When applied to sections of plant drugs, the section is mounted in 1 drop of the α-naphthol solution; 2 or 3 drops of concentrated sulfuric acid are added and the whole is covered with a cover-glass. Sections containing soluble carbohydrates react within two minutes. Insoluble carbohydrates usually require several minutes and occasionally one-quarter to one-half hour.

If the above reaction is carried out using a solution of thymol instead of α-naphthol a brick-red to carmine-red color will be obtained.

The Flückiger Reaction.—Of the many microscopic adaptations of what is commonly known as the Fehling reaction, that proposed by Flückiger is probably the most satisfactory. A small fragment of copper tartrate is dissolved in a few drops of 15 per cent sodium hydroxide solution on the slide, the section introduced (or a drop of the aqueous extract added) and covered with a cover-glass.

Levulose, if present, will cause the precipitation of reddish yellow copper oxide without heating, the precipitate being well localized (in sections). The application of a very little heat will result in further precipitation if dextrose is present. If sucrose is present prolonged heating will cause its change to invert sugar, with the consequent further precipitation of copper oxide.

While the reduction of alkaline copper solutions is a useful reaction it must be borne in mind that other substances besides sugars (some tannins, phenols, etc.) will cause a similar reduction.

The Phenylhydrazine Reactions.—Two reagents are prepared as follows: (1) Phenylhydrazine hydrochloride in glycerin 1 to 10. (2) Sodium acetate in glycerin 1 to 10. One drop of each solution is transferred to a slide and mixed; the section (or a drop of the aqueous extract) is then introduced and the whole covered with a cover-glass. If the slide is allowed to remain at room temperature, levulose, if present, will crystallize out in the form of its osazone after a few hours. Dextrose will form its osazone only after one or more days, while sucrose will form no osazone unless the preparation is heated.

If, for example, a preparation which has remained at room temperature shows no crystals after two days, is heated for thirty to forty minutes on the water-bath and crystals then result, sucrose is thereby indicated. (The phenylhydrazine hydrochloride solution is acid enough to invert the sucrose.) If crystals form at room temperature and then an additional crop of crystals is obtained upon heating, the presence of both mono- and disaccharides is indicated.

If heat is employed with the monosaccharide reaction, crystallization will proceed much more rapidly.

With sections, however, this is disadvantageous, as the carbohydrates will migrate, and not remain localized in their original cells. If heat is used at the beginning of the reaction, no differentation between dextrose, levulose and

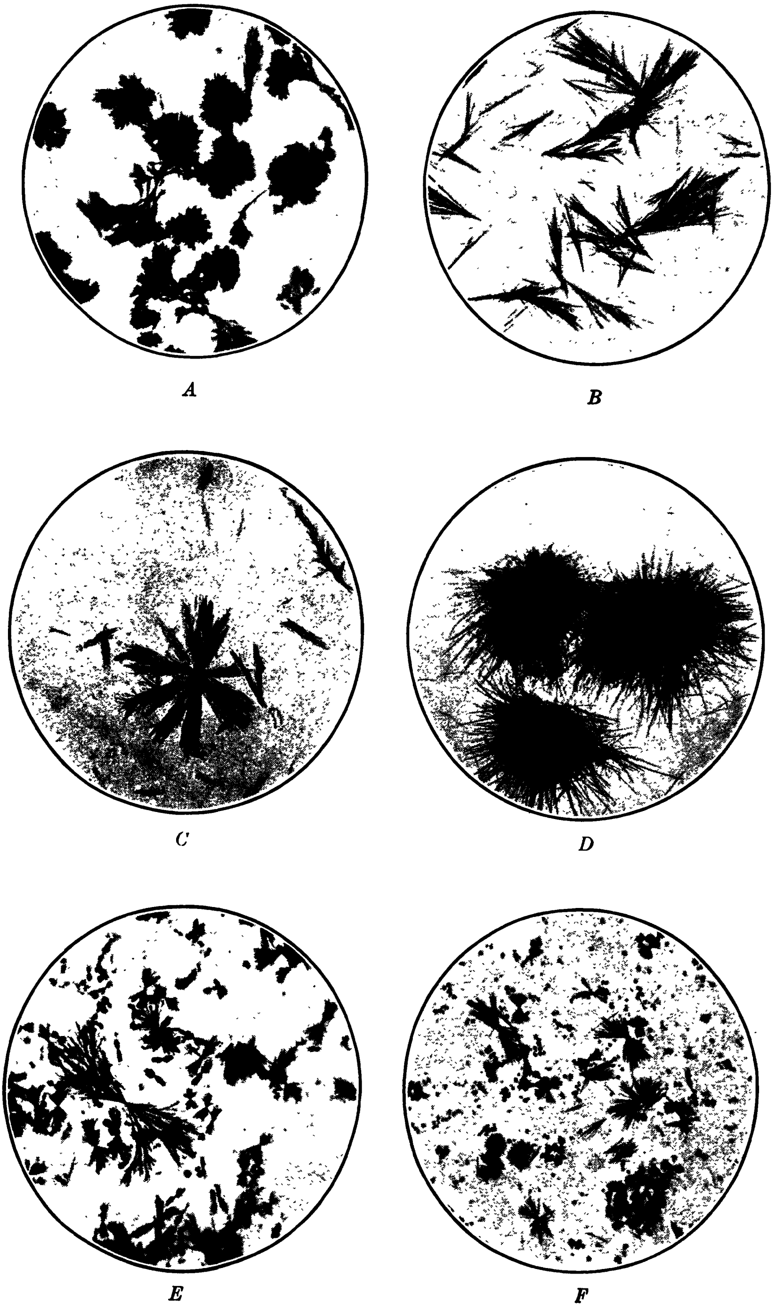


FIG. 48.—Photomicrographs of *A*, Glucosazone; *B*, Fructosazone; *C*, Maltosazone; *D*, Lactosazone; *E*, Osazones from honey; *F*, Osazones from date.

sucrose can be made. The osazone crystals usually occur as sphæro-crystals, or in needles arranged in tufts, sheaves or in star formation (see Fig. 48). Senft, who originally devised the method was able to obtain osazones from fruits and other plant parts. The osazones may be kept as permanent mounts in glycerin-jelly.

Care should be exercised in interpreting results. If glucosides are present and heat is employed they may be hydrolyzed. In such cases the reaction does not indicate the presence of hexoses as such in the plant material under investigation. It should be noted, also, that in the process of drying a drug there is apparently some enzymatic action which will bring about the hydrolysis of glucosides, if present.

Graefe has developed an interesting method for the detection and differentiation of sugars in plant tissue. He found that secondary asymmetrical methylphenylhydrazine will give osazones only with the ketoses. The reaction is thus a specific one for levulose. By combining the results of both reactions, the presence or absence of certain sugars may be readily determined.

Dextrose, levulose and sucrose are the only sugars occurring free in plant tissues. Maltose, which is only found in rare cases, is a reducing sugar, reducing Fehling's solution but not as easily as glucose. It forms osazones with phenylhydrazine but not with methyl-phenylhydrazine. Upon hydrolysis it yields dextrose which may be determined by the above methods. Lactose, which is considered under the section on "Animal Drugs," reduces Fehling's solution and forms an osazone.

The Barfoed Test.—This test is used to distinguish between mono- and disaccharides. Two or three drops of the reagent consisting of cupric acetate, 13.3 gm.; glacial acetic acid 1.8 cc. and distilled water, 200 cc. is placed on the slide which is then transferred to the water bath. Place the section (or drop of the aqueous extract) in the drop noting the time of the addition. Again note the time of the first formation of a reddish brown precipitate. At the same time prepare and process a blank slide having only the reagent.

Solutions of galactose, dextrose or levulose afford strong precipitates, usually within one and a half to two minutes. Maltose and lactose may show some precipitation in about four minutes, while sucrose remains negative for ten minutes or more.

The Seliwanoff Test.—This test is used to indicate the presence of ketose sugars and also to distinguish between ketose and aldose sugars. One to two drops of the reagent consisting of 0.05 gm. of resorcinol in 100 cc. of HCl (1 to 2) are placed on a slide, on the water bath. The section or aqueous solution(1 to 2 drops) are added and the time of addition carefully noted. A blank may also be run and a white background will aid materially in the observation of the color. Note carefully the time of appearance of the first rose-pink color.

Fructose (10 per cent solution) produces a rose-pink color in thirty to forty-five seconds. Sucrose produces the same color in fifty to seventy-five seconds; requiring this additional time for hydrolysis. Glucose and maltose may produce faint pink colors in from three to four minutes, while lactose is usually negative after five minutes. The ketose is converted into levulinic acid and hydroxymethyl-furfural, this latter compound condensing with the resorcinol to form the red-colored compound.

The Mucic Acid Test.—This test is used to demonstrate either lactose or galactose or both; alone or in mixtures. To 1 cc. or less of the sugar solution in a small test-tube, add an equal volume of concentrated nitric acid, stopper the tube and allow to stand for twenty-four hours. Lactose or galactose undergo oxidation to mucic acid, which slowly precipitates in crystalline form which may be identified microscopically.

Glucose and fructose and the non-galactose-containing disaccharides are oxidized to the isomeric saccharic acid, which is water-soluble. Better results are sometimes obtained by the use of fuming nitric acid or by heating the test-tube carefully to boiling before setting aside for twenty-four hours.

STARCH OR AMYLUM

The following kinds of starch have been recognized in the U. S. Pharmacopœia and/or in the National Formulary:

Cassava or Tapioca (U. S. P. 1820 to 1882). (See pages 402, 403.)
Sago (U. S. P. 1820 to 1882). (See page 148.)
Maranta (U. S. P. 1820 to 1882; as reagent, U. S. P. and N. F. each 1936 to date). (See page 185.)
Wheat (U. S. P. 1842 to 1894; as reagent, U. S. P. 1882 to 1894). (See pages 120, 122, 124.)
Canna (U. S. P. 1863 to 1882). (See page 120.)
Potato (as reagent, U. S. P. 1882 to date). (See pages 120, 123.)
Corn (U. S. P. 1894 to date; as reagent, U. S. P. 1894 to 1916)

Wheat Starch and Corn Starch were defined until 1916 as "the fecula of the seed;" since then Corn Starch has been defined as the "grains or granules from the fruit or the grain of *Zea mays* Linné."

Zea mays is native to America, and Indian Corn has been found in the tombs of the ancient Peruvians and in the mounds of the Aztecs of the Mississippi Valley. Columbus took samples of corn to Spain on his return in 1502 and within a very short time it spread over southern Europe, northern Africa and western Asia. The central United States produces the greatest quantity of our domestic supply, Illinois and Iowa leading in this production.

PREPARATION.—Corn grains are softened by being kept for about forty hours in warm water containing enough sulfur dioxide to prevent fermentation. The softened and swollen kernels are then passed through attrition mills which loosen the hulls and break up the starchy endosperm. At this point the germ (embryo) is separated, being subsequently expressed for the oil. The endosperm is further broken up in burrstone mills, and the fine starch and gluten slurry washed away from the non-friable hulls on sieves made of silk bolting cloth into long, slightly inclined, wide-bottom troughs; the starch settles to the bottom and the gluten forms a layer on top. Repeated treatments with cold water give a starch free from practically all gluten. Such starch is known as acid-washed and constitutes almost wholly the corn starch of commerce. The starch is allowed to settle from the last wash water or is filter-pressed and is then dried.

DESCRIPTION.—See pages 120, 122, and 123 and the U. S. Pharmacopœia.

STANDARDS AND TESTS.—Starch is colored a deep blue by iodine T.S. One gram of starch boiled with 15 cc. of distilled water and subsequently cooled results in a translucent, whitish jelly. Starch should contain only a trace of foreign organic matter, should yield not more than 0.5 per cent of ash and not more than 14 per cent of moisture.

USES.—Starch is a nutrient, demulcent, protective and absorbent. It has been used externally to allay itching in erysipelas and urticaria. A starch suspension may be swallowed as an antidote to iodine poisoning. It is used pharmaceutically as a dusting powder and as a diluent for powders. Glycerite of starch is used as an emollient and as a base for suppositories. Starch has many commercial uses such as paper sizing, cloth sizing, laundry starching, etc. It is the starting product from which glucose (corn syrup), dextrose and dextrins are made.

SUGARS

The following sugars have been recognized in the U. S. Pharmacopœia and/or in the National Formulary:

Glucose (U. S. P. 1916 to date).
Dextrose (U. S. P. 1926 to date; in culture media, U. S. P. 1916 to date; N. F. 1926 to date).
Arabinose (in culture media, N. F. 1936 to date).
Xylose (in culture media, N. F. 1936 to date).
Rhamnose (in culture media, N. F. 1936 to date).
Mannitol or Manna Sugar (in culture media, N. F. 1936 to date).
Sucrose or Saccharum (U. S. P. 1820 to date; as reagent, U. S. P. 1926 to date; N. F. 1936 to date).
Maltose (in culture media, N. F. 1936 to date).
Lactose (U. S. P. 1863 to date; in culture media, U. S. P. 1916 to 1926, 1942 to date; N. F. 1926 to date).
Galactose (in culture media, N. F. 1942 to date).
Dulcitol or Dulcose (in culture media, N. F. 1936 to date).

The three latter items are derived from milk, and are described on pages 687 to 688.

Liquid Glucose or Glucose is a product obtained by the incomplete hydrolysis of starch. It consists chiefly of dextrose, maltose, dextrins and water.

In the United States, Liquid Glucose is usually made from corn starch (see page 133). The washed starch is mixed with diluted hydrochloric acid and heated for twenty-two minutes at about 30 pounds pressure; the acid is neutralized; the neutral liquid centrifuged and filtered until clear; then evaporated to the syrupy condition.

It is unfortunate that the name "glucose" has also been applied to pure dextrose.

Description and Properties.—A colorless or yellowish, thick, syrupy liquid; nearly odorless; taste sweet. For Tests of Identity and Purity see the U. S. Pharmacopœia.

Uses.—Glucose is a food and is employed as a sweetening agent, as a substitute for sucrose in syrups, and as an excipient for pills.

Dextrose or d-Glucose is a sugar usually obtained by the hydrolysis of starch. It occurs naturally in grapes and other fruits and may be obtained from these sources as well as by the hydrolysis of certain natural glucosides. It is usually prepared in a manner similar to that of glucose; the conversion takes place after heating at 45 pounds pressure for about thirty-five minutes. The sugar is crystallized, washed and dried to yield a dextrose of 99.5 to 100 per cent purity.

Description, Constants and Tests of Identity and Purity.—See the U. S. Pharmacopœia.

Uses.—Dextrose is a food and may be given by mouth, by enema, by subcutaneous or by intravenous injection. It is used commercially in the manufacture of candy, carbonated beverages, ice cream, bakery products, and in the canning industry.

Calcium Gluconate (U. S. P. 1936 to date) is the calcium salt of gluconic acid. Gluconic acid is obtained by the oxidation of dextrose, either with chlorine, or electrolytically in the presence of a bromide, or by fermentation. Calcium gluconate is soluble in cold water and is less irritant for intramuscular use than calcium chloride. It is used to obtain the therapeutic effects of calcium.

Calcium Levulinate (N. F. 1946 to date) is the calcium salt of levulinic acid. Levulinic acid is prepared from starch or from cane sugar by boiling with hydrochloric acid. The salt is very soluble in water. It is used in subcutaneous injections to obtain the therapeutic effects of calcium.

Levulose, d-Fructose or Fruit Sugar is a ketose occurring naturally in most sweet fruits, and in honey. It is usually prepared by the hydrolysis of sucrose, when it is formed in equal quantity with dextrose, or by the hydrolysis of inulin. It is freely soluble in water, alcohol or acetone and has a specific rotation of −93°. It is used as a food for diabetics and in infant feeding formulas.

Arabinose, l-Arabinose or Pectin Sugar is a pentose obtained from gums such as acacia, mesquite or cherry gum, by boiling the gum with diluted sulfuric acid, thus partially hydrolyzing the arabans present.

It is colorless, odorless, crystallizable, and has a sweet taste. For the **Properties and Tests of Purity** see the National Formulary, Reagent section.

Arabinose is used as a fermentative reagent in culture media.

Xylose, l-Xylose or Wood Sugar is a pentose and is obtained by boiling corn cobs, bran, straw or similar material with dilute acid to hydrolyze the xylans present.

It is colorless, odorless, crystallizable into needles and has a sweet taste. For the **Properties and Tests of Purity** see the National Formulary, Reagent section.

Xylose is very difficult to ferment; it is used for the detection or identification of a certain few, rare species of bacteria, which do ferment it.

Rhamnose, Hydrous l-Rhamnose, Isodulcite or Isodulcitol is a methyl pentose, $C_6H_{12}O_5H_2O$, obtainable from certain glycosides, such as quercetrin, and which are known as rhamnosides.

Rhamnose occurs as colorless, odorless, sweet crystals or a crystalline powder readily soluble in water. The specific rotation of the aqueous solution of the sugar is at first levorotatory (−7°) but soon becomes slightly dextrorotatory (+8.5° to +8.6°).

PROPERTIES AND STANDARDS OF PURITY.—See the National Formulary, Reagent section.

Rhamnose is used as a fermentative reagent in bacteriological culture media.

Mannitol, Anhydrous d-Mannitol, Mannite or Manna Sugar is a hexahydric alcohol obtained from manna or by reduction of mannose. Mannose is a hexose made commercially by hydrolysis of the waste turnings of ivory nuts (vegetable ivory).

Mannitol occurs as a colorless, odorless, sweet powder or in minute crystals. It is soluble in water, reduces Fehling's solution and is fermented by yeast.

Properties and Tests for Purity.—See the National Formulary, Reagent section.

Mannitol is used as a fermentative reagent, as a mild laxative, as a diabetic food and, industrially, in plastics and artificial resins.

Sucrose, Saccharum or Sugar is obtained from sugar cane, *Saccharum officinarum* Linné; sugar beet, *Beta saccharifera* (*vulgaris* Linné) and other sources.

Sucrose is widely distributed in plants, and, commercially, is obtained on a small scale from the sugar maple (*Acer saccharum*, Fam. *Aceraceæ*), from various palms and other sources. Cane sugar is produced in Cuba, Puerto Rico, Louisiana, Philippines, Hawaii, Java and India, while beet sugar is largely produced in Germany, Austria, Russia, France and the United States. The enormous total production of the world is about equally divided between sugar cane and sugar beet.

Sugar cane is native to India, being introduced into Europe by the Venetians during the crusades. During the fifteenth and sixteenth centuries it found its way into most European colonies in the tropics.

Production.—The juice is obtained from sugar cane by crushing the stems between series of heavy iron rollers. It is boiled with lime to neutralize the plant acids (these acids would change the sucrose to invert sugar) and to coagulate albumins. The latter rise to the top as a scum and are removed. The juice is filtered, sometimes decolorized with sulfur dioxide, concentrated and crystallized; when crystals of sugar are no longer obtainable, the residual dark-colored syrup is **Molasses** (U. S. P. 1863 to 1873), which is extensively used in foods, prepared animal foods and in the manufacture of ethyl alcohol.

Description and Properties.—See the U. S. Pharmacopœia.

Uses.—Sugar is a demulcent and a nutrient. In sufficient concentration in aqueous solution it is bacteriostatic and preservative. Pharmaceutically, it is used in syrups and other agreeable vehicles and adjuvants; sugar serves for the masking of disagreeable tastes in troches and tablets, and for the prevention of oxidation in certain preparations of iron.

Maltose, Hydrous Maltose or Malt Sugar is a disaccharide obtained by the partial hydrolysis of starch, usually by means of diastase.

Maltose occurs as colorless, odorless, sweet crystals or a white powder, and is very soluble in water. It is dextrorotatory and is fermented by yeast.

Properties and Standards of Purity.—See the National Formularly, Reagent section.

Maltose is used as an easily digested nutrient, especially in the form of malt extract (see page 138); as a sweetener and as a fermentative reagent.

Caramel or Burnt Sugar Coloring (N. F. 1916 to date) is a concentrated aqueous solution of the product obtained by heating sugar or glucose until the sweet taste is destroyed and a uniform dark brown mass results, a small amount of alkali or alkali carbonate being added while heating.

Description.—Caramel is a thick, dark brown liquid having the characteristic odor of burnt sugar and a pleasant, bitter taste. The specific gravity is not less than 1.30 at 25° C. Caramel mixes with water in all proportions and with aqueous alcohol, having an alcoholic content of less than 80 per cent. One part in 1000 of distilled water yields a clear solution having a distinct sepia tint. Spread in a thin layer, caramel should appear homogeneous, reddish brown and transparent. It should give no precipitate with phosphoric acid and yields not more than 8 per cent of ash.

USES.—Caramel is used in coloring certain pharmaceutical preparations.

ALCOHOL

Alcohol, Ethanol or Spiritus Vini Rectificatus (U. S. P. 1820 to date) is a liquid containing not less than 92.3 per cent by weight, corresponding to 94.9 per cent by volume, at 15.56° C., of C_2H_5OH.

Dehydrated Alcohol or Absolute Alcohol (U. S. P. 1894 to 1946; N. F. 1946 to date; in reagents, U. S. P. 1882 to date) is a liquid containing not less than 99 per cent by weight of C_2H_5OH.

Whiskey or Spiritus Frumenti (U. S. P. 1863 to 1916, 1926 to 1946; N. F. 1946 to date) is an alcoholic liquid obtained by the distillation of the fermented mash of wholly or partly malted cereal grains, and containing not less than 47 per cent and not more than 53 per cent, by volume at 15.56° C., of C_2H_5OH. It must have been stored in charred wood-containers for a period of not less than two years.

The natural processes of fermentation have been utilized since earliest historical times for the making of alcoholic beverages. Fermented beer from grain is mentioned in the Papyrus Ebers (about 1500 B.C.), and fermented grape juice or wine was probably known in prehistoric times. Natural fermentation can hardly produce a concentration of alcohol in the fermenting liquid exceeding 14 per cent by volume, because the fermentative organisms are inhibited at such a concentration.

The process of distillation by which the alcohol in the fermented liquid can be concentrated in the distillate was not known until perhaps the eighth century A.D.

Only in very modern times has the process been so perfected that very pure alcohol could be obtained. By distillation, brandy from wine, whiskey from fermented malted grain and rum from fermented molasses are obtained as commercial articles. Each usually contains from 40 to 55 per cent of alcohol.

DESCRIPTION, CONSTANTS AND TESTS FOR IDENTITY AND PURITY.—See the U. S. Pharmacopœia or the National Formulary under each of the above titles.

OTHER CORN PRODUCTS

Corn Oil (U. S. P. 1936 to 1942; 1947 to date) is the refined, fixed oil expressed from the germ of *Zea mays* Linné.

After the cracked corn leaves the attrition mills (see preparation of *Amylum* page 133) the germs (embryos) are separated by floating out in deep rectangular tanks. After washing free from starch and gluten, the germs are subjected to pressure and heat which expresses the oil. The **germ oil cake** that remains is ground and sold as cattle feed (**oil cake meal**). The crude oil is clarified by filtering and settling, and refined by removing the fatty acids, refrigerating, filtering and sterilizing.

Corn oil is a clear, light yellow oily liquid having a faint characteristic odor and taste. It is slightly soluble in alcohol but miscible with ether, chloroform, benzene and petroleum benzin. Corn oil has a specific gravity between 0.914 and 0.921 at 25° C.; a saponification value between 188 and 193; an iodine value between 112 and 128, and should contain not more than 2 per cent of unsaponifiable matter. The free fatty acids in 10 gm. of corn oil should require not more than 2 cc. of N/10 sodium hydroxide for neutralization and the corn oil should give no reaction for cotton-seed oil.

Corn oil is used as a solvent for irradiated ergosterol and as an emollient. It is an edible oil, and as such is used in salads and cookery. When hydrogenated, the oil becomes semisolid, useful as a shortening in cookery.

Cornsilk or Zea (U. S. P. 1894 to 1905; N. F. 1916 to 1946) consists of the fresh styles and stigmas of *Zea mays* Linné. The styles and stigmas should be collected when the corn is in milk and should be used in the green condition for the manufacture of pharmaceutical preparations.

Styles, slender, very delicate, thread-like, purplish red to greenish white, more or less translucent, 10 to 20 cm. long: stigmas bifid, slender, 0.5 to 3 mm. long; odor slight; taste insipid.

Styles consisting for the most part of parenchyma and two parallel vascular bundles with narrow, spiral, or annular tracheæ; the epidermal cells rectangular, frequently extended into multicellular hairs from 200 to 800 microns in length, the basal portion consisting of two to five united cells, the upper portion usually unicellular; the cells of the hairs are rich in cytoplasm, and each contains a small, spherical nucleus; the purplish red styles contain a purplish red cell sap.

The fresh drug contains about 83 per cent of water. The dried drug contains a volatile alkaloid; two resins about 5.5 per cent; a crystalline principle, maizenic acid, about 1.25 per cent; fixed oil, 5.25 per cent; sugar.

See the National Formulary for standards and tests.

Cornsilk is a diuretic. Average dose, 4 gm.

BARLEY

Barley is the dried grain of one or more varieties of *Hordeum vulgare* Linné. Barley is grown throughout the world wherever the climate is favorable.

Malt or Malted Barley (U. S. P. 1882 to 1894, 1905 to 1936; N. F. 1894 to 1905) is dried, artificially germinated barley grain. To prepare malt, barley grain in heaps in a warm room is kept wet with water and allowed to germinate until the caulicle protrudes. The grain is then quickly dried. The enzyme diastase in the moist warm grains acts to convert the starch to maltose, which stimulates the embryo to growth, and which is killed when the grain is dried.

Dry malt resembles barley, but is more crisp, with an agreeable odor and a sweet taste. It contains 50 to 70 per cent of the sugar, maltose; 2 to 15 per cent of dextrins; 8 per cent of proteins; diastase and a peptase enzyme. Malt yields not less than 70 per cent of dry extract to an aqueous infusion at 50° to 55° C.

Malt is used very extensively in the brewing and alcohol industries. Malt Extract is used medicinally.

Malt Extract (U. S. P. 1882 to 1894, 1905 to 1946; N. F. 1894 to 1905, 1947 to date) is prepared from malt by infusion at 60° C. or less and subsequent concentration at a temperature not exceeding 60° C. Ten per cent by weight of glycerin is added to the extract, which in finished form contains dextrin, maltose, a small amount of glucose, and diastase.

Malt Extract is capable of converting not less than five times its weight of starch into water-soluble sugars.

Malt Extract is used as an easily digested nutritive and as an aid in digesting starch. The average dose is 15 gm. Many commercial extracts of malt contain no diastase, this ferment having been destroyed by the heat used for their sterilization. Such extracts should not be confused with the U. S. P. product.

Diastase (U. S. P. 1916 to 1926) is a yellowish white amorphous powder obtained from an infusion of malt and capable of converting fifty times its weight of potato starch into sugars. Taka-Diastase is a kindred product claimed to convert three hundred times its weight of starch into sugars.

Pearl Barley or Hordeum (U. S. P. 1820 to 1882) is the entire barley grain from which most of the pericarp and seed coat have been removed by passing between two rough revolving plates. Pearl Barley and **Barley Flour** are used as nutrients and demulcents in cases of subnormal digestion.

OAT

Avena or Oat (N. F. 1926 to 1947) is the grain of *Avena sativa* Linné. The plant is extensively cultivated in the United States and Canada, in the northern countries of Europe and in Great Britain. The grain is gathered by threshing which cleans it from the straw.

Oat is pale yellow or pale yellowish-green; up to 1.5 cm. in length and about 3 mm. in diameter, tapering toward each end; the lemma surrounding the grain except on the ventral side where there is a distinct longitudinal groove; outer surface of the lemma glabrous with five or more longitudinal veins on the dorsal surface; within the groove a narrow, thinly membranous, two-veined palet or scale. The fruit or naked grain tapers toward either end; at the micropylar end occurs a wart-like excrescence or caruncle; at the opposite end a dense mass of long slender hairs which also occur, though less abundantly, over the surface of the fruit.

Powdered oat is whitish with a slight odor and a starchy taste. It shows fragments of epicarp with thin-walled cells up to 400 microns in length, with some of the cells extended as slender pointed hairs up to 2 mm. in length and 20 microns in diameter at the base; palet epidermis fragments with coarse unicellular hairs up to 250 microns in length; endosperm cells containing rounded or ellipsoidal, or many-compound starch grains, the compound grains up to 60 microns in diameter, with individual grains polygonal or spindle-shaped and up to 10 microns in diameter.

Oat contains about 43 per cent of starch; a protein, avenin; small amounts of sugar, gum, cellulose, and inorganic salts; total ash about 3.25 per cent; acid-insoluble ash about 1.6 per cent.

Oat is a stimulant and a nutrient.

Avenæ Farina or Oatmeal (U. S. P. 1820 to 1882) is the oat grain deprived of its pericarp and reduced to a granular meal. In more modern times the grain deprived of its pericarp is rolled into flakes or ground to a coarse flour. Cooked with water to a gruel, it offers a palatable, nourishing, easily digested food suitable for convalescents.

RICE POLISHINGS

Rice Polishings, Rice Bran, or Tikitiki (U. S. P. 1942 to date) consist of the fine, flaky pericarp and spermoderm fragments, the embryo, aleurone layer and outer adhering cells of the starchy endosperm of the grain of *Oryza sativa.* Oryza is Greek meaning rice and sativa is from the Latin *sativus* meaning that which is planted, thus indicating cultivated rice. Rice is the staple carbohydrate food of Asiatic peoples and is extensively cultivated in China, British India, Siam and the Philippines. It is also cultivated in our southern states, particularly Louisiana. The rice is hulled between stones, the resulting product being known as "brown rice," which is occasionally found in commerce. The brown rice is decorticated yielding polished rice, the common food product found on the market. Rice polishings are the by-product of this latter operation.

It has long been observed that an exclusive diet of polished rice resulted in the deficiency disease, beriberi. The fact that rice polishings when fed to pigeons with beriberi cured the disease demonstrated that a necessary dietary factor was removed in the polishing process. We now know this to be Vitamin B_1 and probably other members of the B-complex (see page 669). Most of the vitamin content is located in the aleurone layer. Rice polishings are included in the U. S. Pharmacopœia largely because of their use in Philippine medicine. (The U. S. P. is the official Pharmacopœia of the Philippines.)

DESCRIPTION, PHYSICAL PROPERTIES, HISTOLOGY AND IDENTITY.—See the United States Pharmacopœia.

STANDARDS AND TESTS.—Not more than 10 per cent remains on a 30-mesh sieve, indicating a 10 per cent limit on rice hulls. It contains not more than 40 per cent of rice starch, which is determined by the cuprous oxide method.

Rice Polishings Extract (U. S. P. 1942 to date) is a liquid hydroalcoholic extract of rice polishings. One cubic centimeter contains not less than 20 U. S. P. units of Vitamin B_1 and represents approximately 14.5 gm. of polishings. Dose, 8 cc.

TRITICUM

Triticum, Couch Grass or Dog Grass U. S. P. 1882 to 1926; N. F. 1926 to date) consists of the dried rhizome and roots of *Agropyron repens* (Linné) Beauvois. *Agropyron* is from the Greek *agros,* a field, and *pyros,* wheat; *repens* means creeping. The drug was employed to a considerable extent by the ancients as a remedy for urinary disorders. The plant forms slender, jointed rhizomes, by means of which it is extensively propagated.

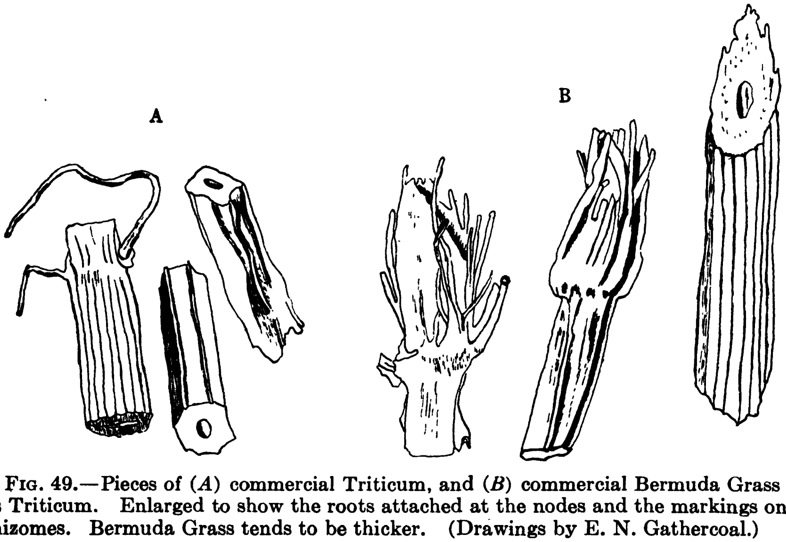


FIG. 49.—Pieces of (*A*) commercial Triticum, and (*B*) commercial Bermuda Grass sold as Triticum. Enlarged to show the roots attached at the nodes and the markings on the rhizomes. Bermuda Grass tends to be thicker. (Drawings by E. N. Gathercoal.)

The rhizome is gathered in spring, usually deprived of the rootlets, cut into pieces and carefully dried. The commercial supplies come chiefly from central Europe, where the plant is indigenous. It has, however, been naturalized in North America.

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 49, 50 and 51 and the National Formulary.

CONSTITUENTS.—Triticin, a lævorotatory carbohydrate resembling inulin, 8 per cent; dextrose and levulose 2.5 to 3.3 per cent; a nitrogenous, gummy substance 11 per cent; acid malates; from 1.85 to 5.2 per cent of total ash and from 0.7 to 1.9 per cent of acid-insoluble ash consisting chiefly of silica from the plant tissues. The rhizome is free from starch and calcium oxalate.

STANDARD OF PURITY.—Triticum contains not more than 2 per cent of foreign organic matter and yields not more than 3 per cent of acid-insoluble ash. Starch grains are few or absent (*Capriola* species).

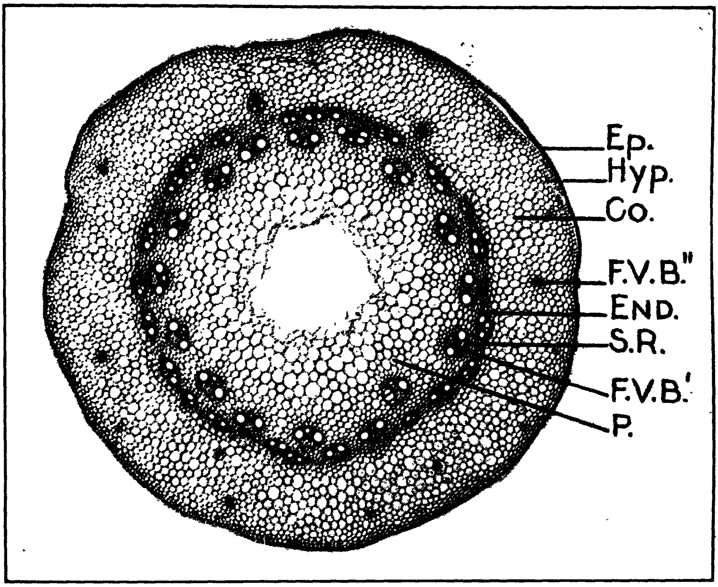


FIG. 50.—Transverse section through the rhizome of *Agropyron repens* (Triticum). *Ep*, epidermis; *Hyp*, hypodermis; *Co*, cortex; *End*, endodermis; *S.R.*, sclerenchyma ring; *F.V.B.'*, fibrovascular bundle; *F.V.B."*, root trace fibrovascular bundle; *P*, pith. (Photomicrograph by R. S. Adamson.)

USES AND DOSE.—Triticum is a demulcent and diuretic. Average dose, 10 gm.

ADULTERANTS.—The rhizomes of various *Carex* species have been reported as adulterants of triticum. They contain starch.

The rhizome of *Capriola dactylon* known as **Bermuda Grass** or **Dog Grass** has been substituted for triticum. It may be distinguished from triticum by many characteristics.

Vetiver, Radix Iwarancusæ or Cuskus Root is the rhizome and roots of *Andropogon squarrosus*, a perennial grass indigenous to the East Indies and cultivated in tropical America and in greenhouses in the United States. The rhizome is short and thick, bearing numerous long, cylindrical, tortuous roots; color, reddish brown; odor, aromatic. A small amount of viscid, dark volatile oil is present, which possesses an intense and very persistent odor, being used primarily in finer perfumery for fixing the more volatile odors. The commercial article is frequently contaminated with red sand, and powdered vetiver with "exhausted" material.

The rhizomes and roots of a number of other *Andropogon* species growing in Brazil and Persia have apparently the same properties as the genuine vetiver.

Citronella Grass, *Andropogon nardus*, is widely cultivated in Ceylon and Java and in Florida and Central America for its volatile oil. The imports of this oil into the United States in recent years have exceeded 1,000,000 pounds per year. **Citronella Oil** is a yellowish green volatile oil having a specific gravity of 0.89 to 0.92 and consists chiefly of geraniol and citronellal. The oil is used in perfumery, especially for soaps. In the form of a spray or by application to the skin it is of value as a protection against mosquitoes and similar insects.

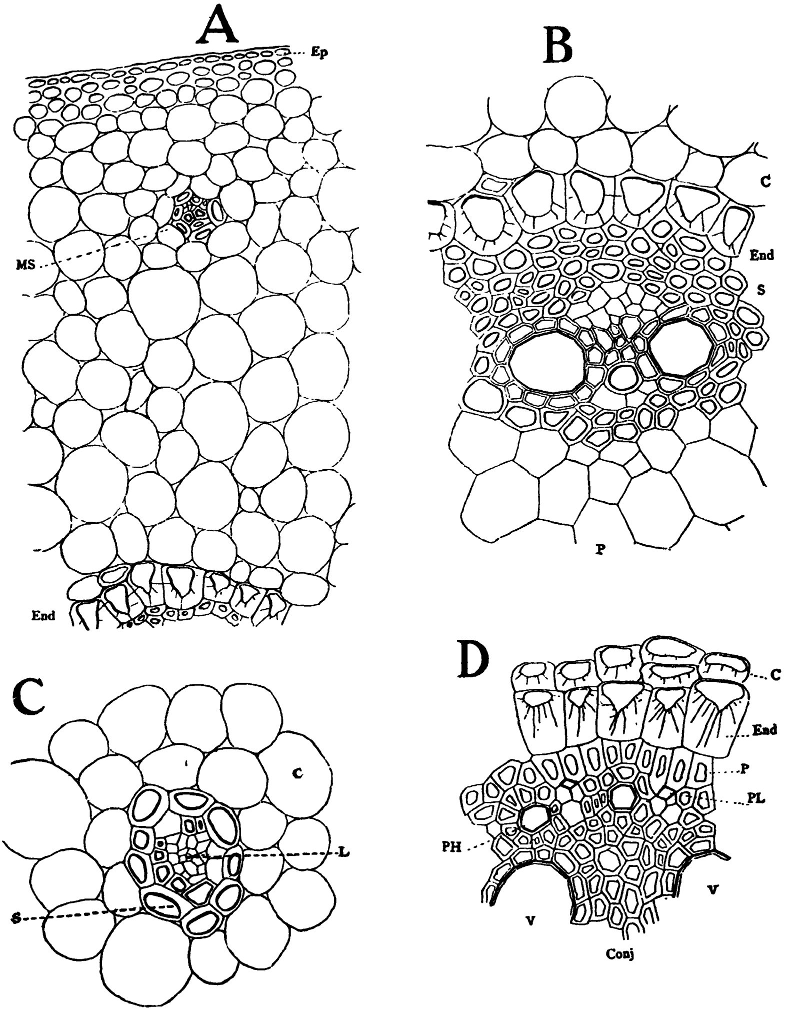


FIG. 51.—Triticum. A, transverse section of a rhizome or stolon; *Ep*, epidermis; *MS*, a vascular bundle situated in the cortical parenchyma; *End*, endodermis. B, continuation of section figures in A: showing cortical parenchyma (*C*); endodermis (*End*); sclerenchymatous fibers or stereome (*S*) surrounding a mestome strand with two large tracheæ having porous walls and small tracheæ with annular thickenings between them; parenchyma cells of pith (*P*). C, a vascular bundle or mestome strand from the cortex (*C*) showing that it is surrounded by a closed sheath of stereome (*S*) and contains almost exclusively leptome. D, transverse section of a portion of a secondary root; *C*, thick-walled cells of inner layer of cortex; *End*, endodermis; *PL*, the protoleptome; *PH*, the protohadrome in which the earliest vessels are developed; *V*, portions of two tracheæ; *Conj*, thick-walled conjunctive tissue. (After Holm.)

Sleepy Grass, *Stipa vaseyi,* grows throughout Mexico and the southwestern part of the United States and possesses the property of causing sleep in any animal that has eaten it. Its marked depressing action on the vital functions of the body obviates the possibility of utilizing its hypnotic properties.

PALMÆ, OR TRUE PALMS

These are mostly shrubs and trees restricted to tropical and subtropical countries. They were at one time quite extensively distributed and very numerous, and at the present time they are represented by about 140 genera and some 1200 species. The trees often reach the height of 100 feet, without branches, and bear at the summit a cluster of large leaves which are either pinnate (feather palms) or palmate (fan palms). The low-growing palms, as the saw palmetto of the southern United States, may have a creeping and branching rhizome. The flowers of palms are produced in the axils of the leaves and are usually unisexual and regular. The carpels may be free or united and develop into a berry (date), drupe (coconut) or nut (betel nut). The seeds have a large endosperm, the cell-walls of which are much thickened with cellulose, as seen in the date and vegetable ivory. The stem consists of an epidermal layer, with silicious walls, and numerous fibrovascular bundles of the concentric type, embedded in parenchyma, so as to form a rather dense woody portion. The palms are of importance to man, being employed for a large number of purposes.

SERENOA

Serenoa, or Saw Palmetto Berries (U. S. P. 1906 to 1916; N. F. 1926 to date) is the partially dried, ripe fruit of *Serenoa repens* (Bartram) Small. The generic name *Serenoa* is given in honor of Professor Sereno Watson, of Harvard; *repens* is Latin signifying "creeping"; that is, producing new plants at a distance from the parent plant; "palmetto" is from the Spanish *palmito,* signifying a small palm tree.

The saw palmetto is a low, scrubby palm found growing from South Carolina to Florida. In some places along the Florida coast the jungles are so thick and the saw-like leaves so dense as to be almost impenetrable. The inflorescence is densely tomentose and shorter than the leaves. The fruit is a 1-seeded drupe (see Fig. 52).

The fruits are partially dried to a prune-like consistence. Some are packed directly in alcohol, which is later employed as a menstruum for their extraction and others are packed in casks, being protected from insect attacks with chloroform or carbon tetrachloride.

Description, Structure and Powder.—See Figure 52 and the National Formulary.

Constituents.—Dextrose, volatile and fixed oils, resins and an enzyme, lipase. The volatile oil is contained in the pulp, and in the fresh fruit is present to the extent of more than 1 per cent. The fixed oil consists of caproic, caprylic, capric, lauric, palmitic and oleic acids and their ethyl esters.

Standards.—Serenoa contains not more than 1 per cent of foreign organic matter and yields not more than 2 per cent of acid-insoluble ash. Serenoa should contain from 10 to 15 per cent of natural moisture when used for the manufacture of pharmaceutical preparations.

Uses and Dose.—Serenoa is a diuretic, sedative and anticatarrhal. Average dose, 1 gm.

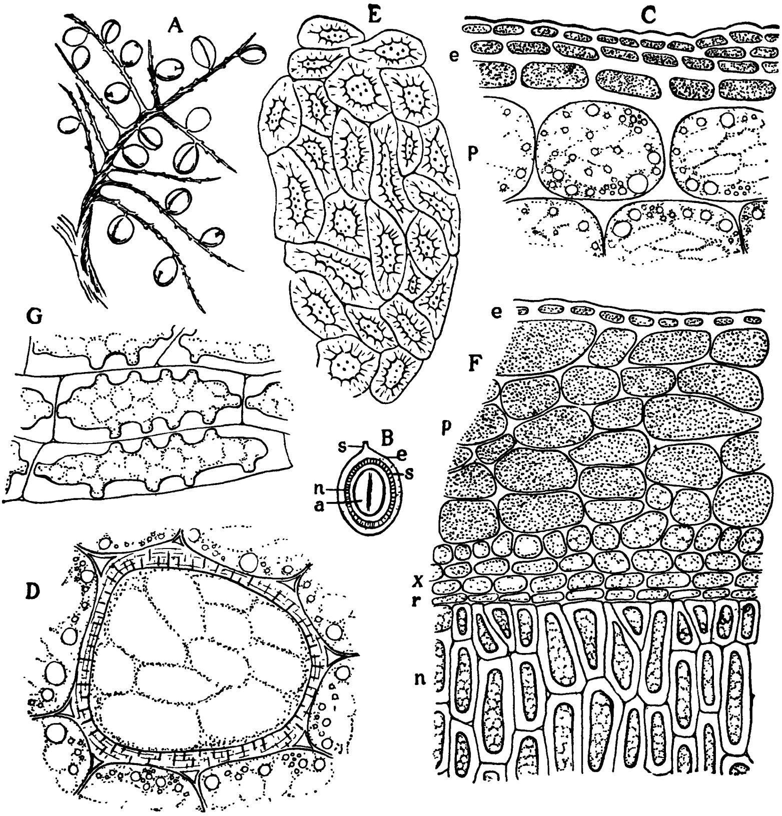


Fig. 52.—Saw palmetto (*Serenoa repens*): *A*, fruiting branch; *B*, longitudinal section of fruit showing short stalk (*s*), epicarp (*e*), sarcocarp (*s*), endocarp (*n*), and anatropous seed with raphé (*a*); *C*, cross-section of outer portion of fruit showing epidermis (*c*), subepidermis (*e*) composed of several layers of cells having a dark reddish brown content, cells of sarcocarp (*p*) with reddish brown content and oil; *D*, a sclerotic cell from the sarcocarp showing the fine radiating pores and concentric lamellæ of the wall; *E*, sclerotic cells from endocarp; *F*, cross-section of portion of seed showing epidermal cells (*e*), large parenchyma cells (*p*), inner epidermis (*x*), perisperm (*r*), endosperm (*n*); *G*, some thick-walled endosperm cells from the inner portion of seed.

ARECA

Areca, Areca Nut or Betel Nut (N. F. 1936 to date) is the dried ripe seed of *Areca catechu* Linné. *Areca* is the Spanish and Portuguese term for the betel nut. *Catechu* is the East Indian name for an astringent extract or juice. *Areca catechu* is a beautiful tall palm extensively cultivated in India, southeastern Asia, in the East Indies and to some extent in east Africa. The fruit is a nut containing a single seed with a thin seed coat and a large ruminate endosperm. The seeds are removed from the fruits, boiled in water containing lime, and dried. The principal points of export are Ceylon, Singapore, Penang and Madras.

Areca is mixed with lime, the leaves of *Piper betle,* and occasionally gambir, the mixture being used as a stimulant masticatory in India and the East Indies. In India the mixture is known as "punsupari." Betel chewing has been practiced since early times. The value of areca as a tænicide seems to have been known in the East for some time but was not known to western civilization until 1863.

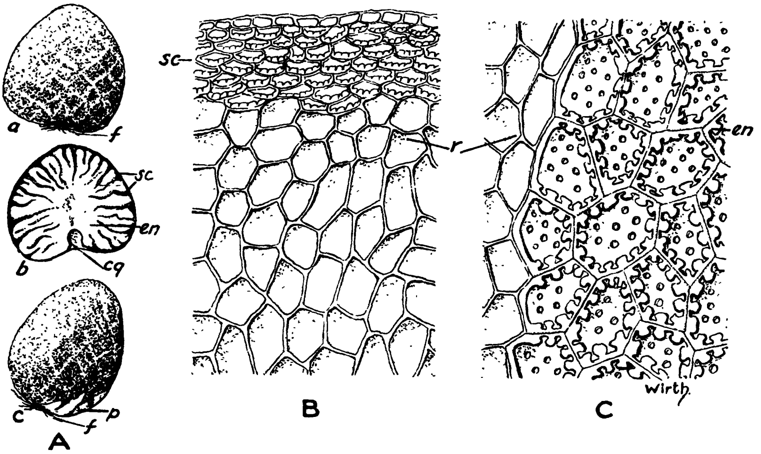


FIG. 53.—*Areca catechu.* *A*, entire rounded conical seeds (up to 3 cm. long and 2 cm. in diameter), brownish, showing a network of paler lines (*a,c*), occasional adhering patches of silvery, brittle endocarp (*p*), and adhering fibers of the mesocarp (*f*); longitudinally cut seed (*b*), showing a marbled appearance of alternating dark brown seed coat (*sc*) and whitish endosperm (*en*) (ruminate endosperm), and the cavity (*ca*) near the base containing the embryo. *B*, transverse section of the seed near the periphery showing seed coat (*sc*) of several rows of tangentially elongated lignified cells with the inner walls more or less thickened, and rumination tissue (*r*). *C*, transverse section from the inner portion of the seed showing rumination tissue (*r*) adjacent to the endosperm (*en*), the latter consisting of cells having thick, porous walls of reserve cellulose. (Drawing by Wirth.)

DESCRIPTION AND STRUCTURE.—See Figure 53 and the National Formulary.

POWDER.—Weak reddish brown to light brown with a slight odor and an astringent, slightly bitter taste. It consists principally of fragments of the endosperm with porous, reserve-cellulose walls; irregularly thickened stone cells of the seed coat; a few aleurone grains up to 40 microns in diameter and a few oil globules; starch absent and tracheal tubes few.

CONSTITUENTS.—Areca contains several alkaloids which are reduced pyridine derivatives; among them guvacine (tetrahydro-nicotinic acid), arecaidine (tetrahydro-methylnicotinic acid), and arecoline (arecaidine methyl ester). Arecoline, 0.1 to 0.5 per cent, only, is of medicinal importance. It is a liquid boiling at 220° C. Homoarecoline (arecaidine ethyl ester) occurs as colorless crystals with the same activity as arecoline but perhaps less toxic. A red phlobatannin, and about 14 per cent of a fixed oil are also present.

To demonstrate arecoline in areca, place a dry-cut section in a small drop of diluted hydrochloric acid (1 in 10) on a slide. The drop should be just large enough to moisten the section and cause it to roll out flat. Cover with a cover-glass and run a few drops of potassium bismuth iodide (Kraut's reagent) under the cover-glass. Reddish brown spheres will form in the endosperm cells, at the edge of which crystallization in plates will be seen. Crystals are formed in the endosperm cells only, not in the cells of the rumination.

STANDARDS.—Areca contains not more than 2 per cent of adhering pericarp and not more than 1 per cent of other foreign organic matter, and yields not less than 0.35 per cent of ether-soluble alkaloids calculated as arecoline and not more than 2.5 per cent of total ash.

USES AND DOSE.—Areca finds its principal usage in veterinary practice, being employed as a vermicide and tænifuge. Average dose: dogs, 2 to 4 gm., sheep, 4 to 8 gm., based on the weight of the animal.

Arecoline Hydrobromide (N. F. 1936 to date) occurs as a white crystalline powder or in fine needle-like crystals having a melting-point of 170° to 175° C. It is odorless and has a bitter taste. Arecoline hydrobromide is soluble in water and alcohol, the aqueous solution being optically inactive.

TESTS AND STANDARDS.—Arecoline hydrobromide responds to the test for bromide; yields a red-brown precipitate with iodine and a yellow precipitate with bromine. When dried over sulfuric acid for twenty-four hours, it loses not more than 1 per cent in weight. It yields not more than 0.5 per cent of ash and should be free from other alkaloids and from sulfate.

USES AND DOSE.—Arecoline hydrobromide has been used in veterinary medicine for colic in horses. It is also a tænicide and a myotic. Average dose: horses, 30 mg. subcutaneously; dogs, 1.5 mg. per kg. of body weight.

COCONUT

The **Coconut Palm** (*Cocos nucifera*) grows in the coast regions of all tropical countries and is most useful to the natives, furnishing food, clothing, utensils of all kinds, building materials, etc. It is a tall stately tree rising to the height of 100 feet, with a tuft of leaves at the top, and among which are borne fruits, often a hundred or more each year. The generic name *Cocos* is from the Greek, meaning "a berry" or "a pill"; *nucifera* is from two Latin words, meaning "nut-bearing."

The following classification of the products obtained from the coconut palm shows its manifold uses:

- Fruit
  - Kernel (copra) for food and expression of fixed oil.
    - Coconut Oil for cooking, soap making, and pharmaceutical uses.
    - Coconut Oil Cake for cattle feed.
  - "Milk" for a nourishing drink.
  - Shell for native household articles.
  - Husk (Coir) fiber for ropes, mats, carpets, brushes, etc.
- Trunk
  - Wood (Porcupine wood) for cabinet work, building and other construction, firewood, etc.
- Leaves for thatching, plaiting, mats, baskets, etc.
- Young Leaves for food.
- Flower Spathe.
  - Juice for a sweet drink.
    - Fermented juice for a liquor (Toddy).
    - Distilled fermented juice for a strong liquor (Arrack).
    - Acid-fermented juice for vinegar.
    - Evaporated juice for palm sugar (Jaggery).

Coconut.—The coconut of commerce is the ripe fruit deprived of its husk (epicarp and mesocarp) thus consisting of the seed covered by the hard stony endocarp to which are attached a few fibers of the mesocarp. In the smaller end of the coconut occur usually three germinating "eyes."

Copra is the ripe kernels (meat) of the coconut, removed and dried in the sun. It yields up to 35 or 40 per cent of fixed oil. Sections of copra show more or less isodiametric cells containing needle-shaped fat crystals and large aleurone grains. Copra, sweetened and cut into shreds forms the **shredded coconut** used in cooking and pastry making.

Coconut Oil (N. F. 1946 to date) is the fixed oil obtained by expression or extraction from the seeds of *Cocos nucifera* Linné.

The fresh kernel contains 30 to 40 per cent of oil; copra yields about 65 per cent of oil. Copra expressed without heat yields first a thinner oil (**copra olein**), then a thicker oil (**copra stearin**). About 1.25 billion pounds of the oil are produced annually.

DESCRIPTION.—Coconut Oil is a pale yellow to colorless liquid at 28° to 30° C.; at 20° C. it becomes semisolid; and at 15° C. it is hard, somewhat brittle and with a characteristic fracture. It may have a faint odor and taste of coconut, but when well purified from free fatty acids, it is odorless and tasteless. It is insoluble in water, but readily soluble in ether, chloroform, carbon disulfide and petroleum benzin. For Constants see the National Formulary.

CONSTITUENTS.—Trilaurin up to 50 per cent; trimyristin, up to 20 per cent; and other glycerides, including tripalmatin, tristearin, triolein, and tricaprylin, the free acid of the latter giving the oil an unpleasant odor. Chemically, it rather closely approximates butter.

USES.—It is extensively used in compounded edible fats, chocolate and candies; in hair dressings and other cosmetics; in soap; in candles and night lights; and pharmaceutically in ointment bases.

Coconut Shells.—The endocarp of the fruit, while used as a household article by the natives, is to some extent ground up and used extensively as an adulterant of powdered foods and drugs. The presence of coconut shells may be detected by their yellow stone cells, which have thick yellow walls with branching pores and dark brown contents. The stone cells vary from polygonal and isodiametric, to cylindrical and wedge-shaped forms that are quite characteristic. In addition there occur fragments of long thick-walled, porous fibers with accompanying stegmatic cells, each containing a spheroidal, tuberculated siliceous granule. The dark brown fragments in the powder are not affected by bleaching agents, such as Schulze's macerating solution.

Coir is the fibers of the mesocarp and is used in the manufacture of rope, brushes, coconut mats and coarse cloth.

OTHER PALM PRODUCTS

Palm Oil.—This is a fixed oil obtained from the fleshy part of the fruit of *Elæis guineensis*, a palm of western Africa, and cultivated in other tropical countries. The oil has the consistency of butter, a reddish yellow color, an agreeable odor and a pleasant taste. It is chiefly used for making soap and in the manufacture of galvanized iron, the oil being spread over the hot iron surface to preserve it from oxidation until it is dipped into the bath of melted tin.

Dragon's Blood, Sanguis Draconis or Resina Draconis.—This is a resin prepared from the fruits of various species of *Calamus* (*Dæmonorops*), particularly *Calamus draco*. These are palms growing in Borneo and Sumatra. The product is a spontaneous exudation from the ripening fruit. It is separated from the fruit, softened with heat and molded into sticks and cakes, which are wrapped in strips of palm leaf. The term "dragon's blood" has been applied to products obtained from other plants, that mentioned by Dioscorides being from a liliaceous plant *Dracæna ambet* growing in Socotra.

Because of its stimulating and astringent properties, it was formerly used in dentifrices, mouth washes, etc., but today it finds use mainly in the preparation of lacquers and varnishes (mahogany stain).

Date.—The date palm, *Phœnix dactylifera* is cultivated in northern Africa, southwestern Asia, Arizona and other tropical countries. It reaches a height of 60 feet, having a crown of pinnated leaves among which are several spadices each of which (on the female tree) bears from 180 to 200 fruits (dates). The trees are artificially pollinated to increase the crop. Dates contain about 47 per cent of invert sugar and are an important article of commerce. In northern Africa, Arabia and Persia they form the chief food and principal wealth of the people.

Sago (U. S. P. 1820 to 1882) consists of the starch prepared from the pith of the trunks of various palms and cycads growing in India and the East Indies, principally *Metroxylon rumphii* and *M. læve.* The pith is separated from the hard outer layers of the trunk, crushed, and the starch washed out on sieves. The characteristics of the starch have already been discussed (see page 120).

Carnauba Wax is obtained from the leaves of *Copernicia cerifera,* a palm ranging from northern Brazil to Argentina. The wax is considerably used in the manufacture of candles, wax varnishes, leather and furniture polishes, and other uses in place of beeswax.

Vegetable Ivory is the ripe subglobular seed, 3 to 5 cm. in diameter, of various species of *Phytelephas,* nearly stemless palms found mostly in Colombia on the bank of the Magdelena River. These hard, white seeds are used for coat buttons and many other turned objects.

ARACEÆ, OR ARUM FAMILY

This family consists mainly of tropical plants characterized by an inflorescence consisting of a spadix placed within a spathe. There are about 900 species, most of them found in tropical and subtropical countries, only about 10 species growing in temperate regions. The latter are mostly perennial herbs possessing rhizomes or acrid corms. The inner morphology is not constant, some genera containing characteristic spicular cells; a few contain tannic acid; others contain oil cells as in calamus, and quite a number contain laticiferous cells. Some of the plants are highly ornamental and are extensively cultivated, as the caladiums.

CALAMUS

Calamus or Sweet Flag (U. S. P. 1820 to 1916; N. F. 1936 to date) is the peeled, dried rhizome of *Acorus calamus* Linné. The specific name *Calamus* means "a reed." The commercial supplies of the drug are obtained from Germany, England, Russia, India, Michigan, Indiana, North Carolina and Virginia. The rhizomes are collected in the autumn, separated from leaves and roots, split longitudinally, and sometimes peeled before drying. During drying the rhizome shrinks considerably and loses about 75 per cent of its weight. Both peeled and unpeeled drug is found on the market but only the peeled is official, though unpeeled drug yielding not more than 2 per cent of acid-insoluble ash and meeting other conditions of the monograph may be used for extractive preparations. A confection is also made by "candying" the fresh rhizomes. The drug was employed in India in ancient times and was also known to the Greeks and Romans. The time of its introduction

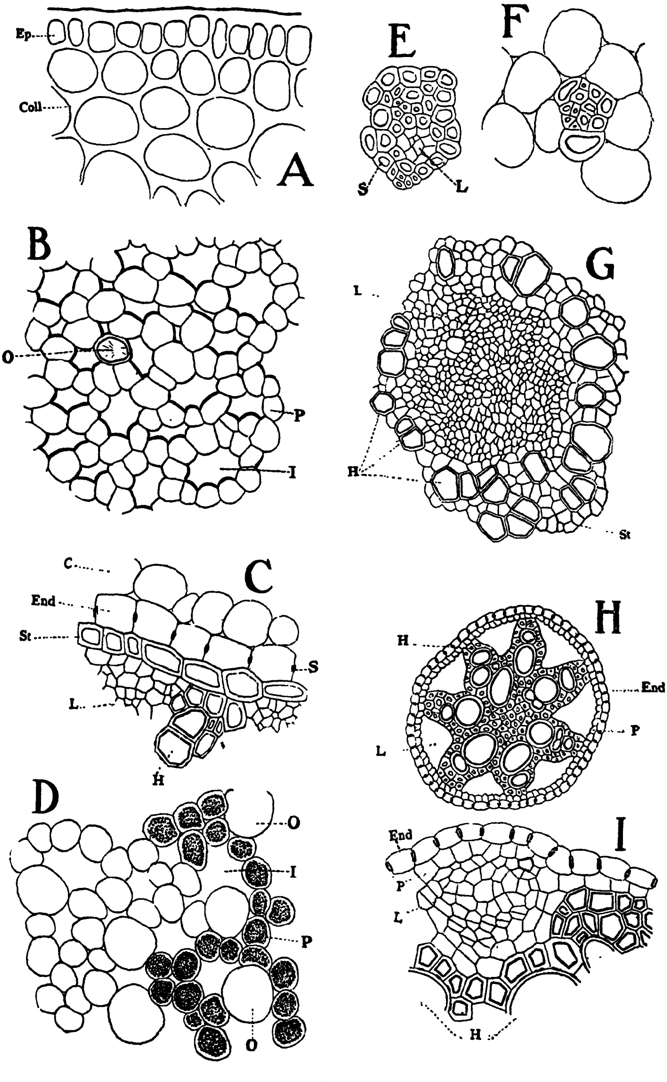


FIG. 54.—*Acorus calamus:* Figs. **A** to **G**, from transverse section of the rhizome; **H** and **I**, of the root. **A**, epidermis (*Ep*) and collenchyma (*Coll*) from rhizome (absent in the official drug). **B**, cortex and **D**, pith, composed of isodiametric, thin-walled, starch-filled parenchyma (*P*) in chains surrounding large intercellular air spaces (*I*), each chain containing one or more larger, spheroidal secretion sacs (*O*) with a yellowish volatile oil content. **C**, endodermis cells (*End*) with thin walls and casparyan spots (*S*); pericycle (*St*) of lignified, thick-walled cells; phloem (*L*) and xylem (*H*) portions of the V-shaped collateral bundle adjacent to the pericycle. **G**, a leptocentric bundle showing phloem (*L*), tracheæ (*H*), and sclerenchymatous fibers (*St*). **E**, the same type of bundle as G, but reduced to phloem (*L*) and fibers (*S*). **F**, the same type of bundle further reduced to fibers only. **H**, the radial bundle of the root, with the phloem strands at (*L*), the xylem strands at (*H*), and surrounded by the pericambium (*P*) and endodermis (*End*) **I**, from the same radial bundle but more highly magnified. (After Holm.)

into Europe is not known but it seems to have been used as early as the sixteenth century.

DESCRIPTION, STRUCTURE AND POWDER.—See Figure 54 and the National Formulary.

CONSTITUENTS.—Volatile oil 1.5 to 3.5 per cent; acorin, a bitter, viscid aromatic glycosidal principle, which when hydrolyzed in a current of hydrogen yields oil of calamus; choline (trimethyl-hydroxy ethyl ammonium hydroxide), a strong, non-poisonous base, formerly known as calamine; a soft resin about 2.3 per cent; tannin; mucilage; starch and calcium oxalate. Total ash about 4.35 per cent; acid-insoluble ash about 0.15 per cent.

STANDARDS AND TESTS.—Calamus yields not less than 1.2 cc. of volatile oil of calamus from each 100 gm. of drug. It contains not more than 1 per cent of foreign organic matter, not more than 6 per cent of total ash and not more than 0.5 per cent of acid-insoluble ash. Powdered calamus contains no starch grains over 10 microns in size (cereal flours and althea).

USES AND DOSE.—Calamus is a carminative, a stimulant and an aromatic bitter tonic and is used as a flavoring agent. Average dose, 3 gm.

Arum, Indian Turnip or Jack-in-the-Pulpit (U. S. P. 1820 to 1873) is the corm of *Arisæma triphyllum*, a common plant growing in rich woods in eastern North America. The corms are gathered, cut transversely into pieces and dried. It contains a volatile acrid principle, probably an alkaloid; mucilage; and calcium oxalate in long raphides. Arum is used as a stimulant, expectorant, irritant and diaphoretic.

European Arum, or Tubera Ari is the corm of *Arum maculatum*, a perennial herb growing in central and southern Europe. The corms are gathered in the spring, sliced transversely and dried. The constituents and properties are similar to those of Indian turnip.

Dracontium or Skunk Cabbage (U. S. P. 1820 to 1882) is the dried rhizome and roots of *Symplocarpus fœtidus*, an herb indigenous to moist ground in North America. It contains volatile oil, resin and an acrid principle and is used to some extent as an antispasmodic, emetic and diuretic.

Tonga is a mixture of equal parts of the root of *Epipremnum pinnatum* (Fam. *Araceæ*) and the bark of *Premna arborea* (Fam. *Verbenaceæ*) and is described on page 522.

LILACEÆ, OR LILY FAMILY

These are mostly perennial herbs having bulbs or tubers and rarely fibrous roots. There are about 200 genera and 2600 species and they are found in nearly all portions of the globe. A few are used in medicine, some furnish food products, but their chief interest is in their ornamental uses. The leaves are for the most part parallel-veined and the flowers are regular and with 6 stamens, and a superior (rarely inferior) trilocular ovary. There are no striking anatomical characteristics; the fibrovascular bundles are concentric and arranged in several rows, outside of which and within the endodermis is a ring of sclerenchymatous fibers. The underground organs usually contain starch and not infrequently mucilage cells enclosing raphides.

VERATRUM VIRIDE

Veratrum Viride, American or Green Hellebore (U. S. P. 1820 to 1942; N. F. 1942 to date) consists of the dried rhizome and roots of *Veratrum viride* Aiton.

Veratrum is from the Latin *vere* meaning truly, and *ater* meaning black; *viride* is Latin, meaning green. The plant is found growing in wet meadows in the mountainous sections of New England and the eastern United States, south to North Carolina, Tennessee and northern Georgia. Most of the commercial drug is collected in New York State south to the Pennsylvania line. The rhizomes are dug, cleaned, cut longitudinally and dried. The drug was known to the Indians who probably introduced its use to the early settlers.

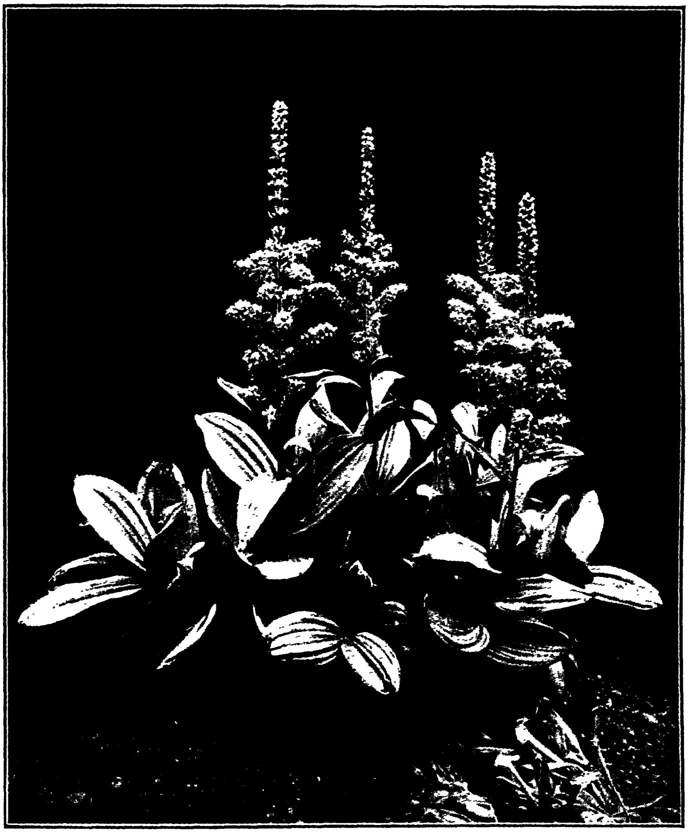


FIG. 55.—Plants of *Veratrum viride* growing in the Royal Botanic Society's Gardens (London) and showing the parallel-veined (or nerved) leaves with entire margin and the large terminal panicles of flowers. (After Pérrédès.)

European or White Hellebore (U. S. P. 1820 to 1882) is the rhizome of *Veratrum album*, a plant similar to *Veratrum viride*, but indigenous to central and southern Europe. Much of the green hellebore used in America is obtained from *Veratrum album* and imported from Germany.

DESCRIPTION AND HISTOLOGY.—See Figure 56 and the National Formulary. White hellebore is similar in appearance and structure to green hellebore, but the external color is much lighter.

POWDER.—Grayish brown to dark brown; strongly sternutatory; taste bitter and acrid (see Fig. 56).

Constituents.—Four alkaloids have been isolated from both varieties: (1) protoveratrine (about 0.03 per cent); (2) jervine (about 0.13 per cent); (3) pseudojervine (about 0.04 per cent) and (4) rubijervine (about 0.025 per cent). These alkaloids vary in toxicity, protoveratrine being the most toxic. No one of them alone exerts the same action as the drug. Cevadine (crystalline veratrine) has been reported in both varieties but this requires further confirmation.

Standards.—Veratrum Viride contains not more than 5 per cent of its stems or other foreign organic matter and yields not more than 4 per cent of acid-insoluble ash. A bioassay using **Daphnia** as the test animal is used in standardizing preparations of Veratrum Viride.

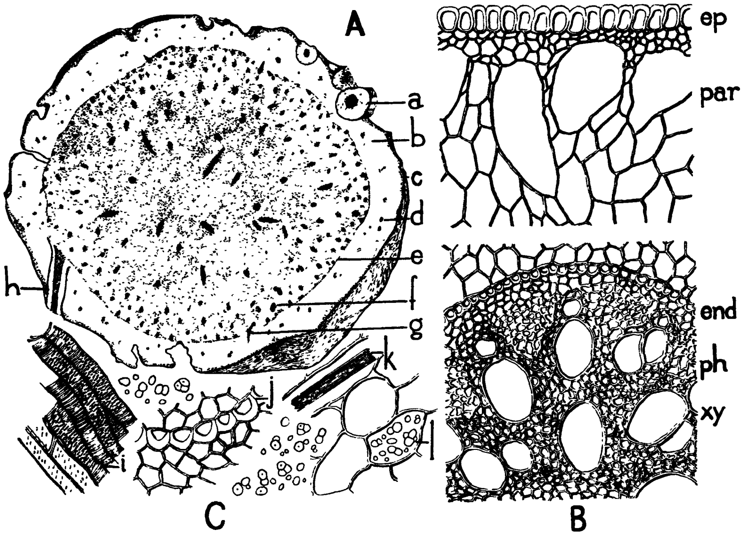


Fig. 56.—*Veratrum viride.* *A*, transverse section of the rhizome: *a*, section of a root near its origin in the rhizome; *b*, the cortex with an outer layer (*c*) of brownish cork-like cells, numerous fibrovascular bundles (*d*) often cut obliquely, and parenchyma containing raphides of calcium oxalate and starch; (*e*) endodermal layer occasionally broken by leaf-trace bundles (*g*) or root bundles (*h*); *f*, vascular bundles of the central cylinder in interrupted circles, or scattered throughout the central parenchyma. *B*, some tissues from the transverse section of the root: *ep*, epidermal cells with lignified thickened outer and radial walls; *par*, parenchyma similar to that of the rhizome, but interspersed with large irregular cavities in the outer regions of the root cortex; *end*, endodermal cells with inner and radial walls thickened and lignified. The central fibrovascular radial bundle contains from 6 to 15 xylem (*xy*) rays and as many alternating phloem (*ph*) strands. *C*, elements of the powder: starch grains (*l*) numerous, from 3 to 20 microns in diameter, spheroidal or ellipsoidal, single or 2- to 3- compound, the individual grains having a circular central cleft and often being swollen or otherwise more or less altered; calcium oxalate (*k*), in raphides from 15 to 150 microns in length; fragments with tracheæ (*i*), the walls being more or less strongly lignified and marked with scalariform or reticulate thickenings, frequently containing a lemon-yellow substance and associated with narrow, slightly lignified, porous, sclerenchymatous fibers; endodermal cells of the rhizome (*j*) thickened on the inner tangential wall; occasional reddish brown or brownish black cork fragments. (Drawing by Florence Carpenter.)

Uses and Dose.—Veratrum Viride is a cardiac depressant and a sedative; it slows the heart and lowers blood pressure and it has shown considerable value in the treatment of hypertension. Average dose, 100 mg. The powdered hellebore used as an insecticide by gardeners may consist of either white or green hellebore, though usually the former.

ADULTERANTS.—Sand and dirt to the extent of 25 per cent or more may be present in white hellebore.

The rhizome of *Veratrum viridifolium*, a plant with greenish flowers growing in the mountainous districts of Europe and northern Asia, contains jervine and veratroidine. The rhizome of *Veratrum nigrum*, a plant with purplish red flowers, indigenous to middle and eastern Europe, Siberia, Manchuria and Japan, contains jervine. *Veratrum californicum*, of the western United States, is very similar to *V. album*, possibly a transitional form between *V. album* and *V. viride*.

Sabadilla (U. S. P. 1842 to 1882) is the seed of *Schœnocaulon officinalis*, a bulbous plant indigenous to Mexico and the West Indies. The seeds are brownish black, 5 to 8 mm. long, narrow, angular, beaked, with a bitter and acrid taste. They contain about 1 per cent of a mixture of alkaloids.

Veratrine (U. S. P. 1842 to 1916; N. F. 1926 to 1936) is a mixture of alkaloids obtained from the seed of *Schœnocaulon officinalis*. The drug consists of cebadine, cevadilline, sabadine and sabadinine. A decoction of sabadilla seed or ointment prepared from veratrine is used to destroy body lice.

Black Hellebore has sometimes been sold under the name of American Hellebore. The drug is a powerful cardiac stimulant and its substitution for veratrum viride may be very dangerous because of the directly opposite therapeutic effect. It may be readily distinguished by its grayish black color, its knotty appearance and its dicotyl structure (see page 250).

COLCHICUM

Colchicum Corm (U. S. P. 1820 to 1936; N. F. 1936 to date) is the dried corm of *Colchicum autumnale* Linné.

Colchicum Seed (U. S. P. 1831 to 1946; N. F. 1946 to date) is the dried ripe seed of *Colchicum autumnale* Linné.

Colchicine (U. S. P. 1905 to date) is an alkaloid obtained from *Colchicum autumnale* Linné.

The genus name is from Colchis on the Black Sea, where the plant flourishes; *autumnale* refers to the season when the plant blooms. The plant is cultivated in England, central and southern Europe and northern Africa, growing in moist meadows. It is now cultivated also in Washington, Oregon and northern California. Two to six flowers having long perianth tubes develop from the corm buds in the fall, the fertilized ovary remaining underground during the winter, and developing the fruit above ground along with the leaves the following spring and summer. The seed is collected in July and August and the corm in the spring before leaf development.

Dioscorides mentions a *Colchicum*. The Arabs recommended the use of the corm for gout in medieval times. It came into usage in Europe about the middle of the seventeenth century and the seed about 1820.

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 57 and 58 and the National Formulary.

CONSTITUENTS.—The alkaloid, colchicine, up to 0.8 per cent in the seed and 0.6 per cent in the corm. The seeds also contain fixed oil (about 6 per cent); proteins; colchicoresin; starch grains in the caruncle; and about 2.5 per cent of total ash. The corm contains much starch and two resins.

STANDARDS.—Colchicum Seed yields not less than 0.45 per cent of colchicine, and not more than 1 per cent of acid-insoluble ash. Colchicum Corm yields not less than 0.25 per cent of colchicine and not more than 0.5 per cent of acid-insoluble ash.

USES AND DOSE.—Colchicum is an alterative, a sedative and a diuretic. It is used chiefly as an antirheumatic in gout and rheumatism. Average dose of the seed 200 mg.; of the corm 250 mg.

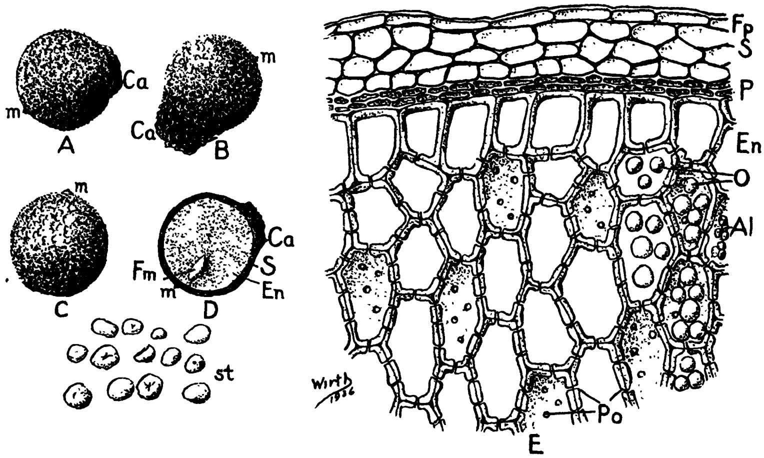


FIG. 57.—Colchicum Seed. *A*, *B* and *C*, ovoid to irregularly globular seeds (2 to 3 mm. in diameter), minutely pointed at the micropyle (*m*) and with a distinct beak or caruncle (*Ca*) which is sometimes absent (*C*). The seeds are dark brown externally, finely pitted, very hard, inodorous, bitter and acrid. When cut longitudinally (*D*) they show a dark brown seed coat (*S*) and a whitish or light brown endosperm (*En*) embedded in which is a small embryo (*Fm*) usually from 40 to 180 degrees from the caruncle. A transverse section of the seed (*E*) shows a seed coat (*S*) usually consisting of six rows of cells, the cells of the outer epidermal row (*Fp*) being somewhat elongated tangentially and cutinized externally. The inner two rows of the seed coat (*P*) are smaller and contain a brownish pigment. The endosperm (*En*) is composed of parenchyma with thick porous (*Po*) walls (except the outer row of cells which exhibit pores only on their inner walls). The cells of the endosperm contain globules of fixed oil (*O*) and aleurone grains (*Al*) from 3 to 15 microns in diameter. Sections through the caruncle show ellipsoidal or rounded starch grains (*St*) from 5 to 20 microns in size. (Drawings by Wirth.)

Colchicine is prepared by exhausting the seed (or corm) with hot alcohol, evaporating the alcohol, taking up in water and shaking out the aqueous solution with chloroform. The chloroform solution yields chloroform-colchicine (see below) upon evaporation; it is then taken up in alcohol, heated to remove the chloroform and finally taken up in ether from which the alkaloid is separated. Colchicine has one aliphatic nitrogen atom.

DESCRIPTION.—Colchicine occurs in pale yellow amorphous scales or in powder which gradually turns darker on exposure to light. One gram is soluble in 22 cc. of water, 220 cc. of ether or 100 cc. of benzene and freely soluble in alcohol and chloroform.

TESTS.—There are no known satisfactory microcrystalline reactions for colchicine. One milligram of colchicine with 2 or 3 drops of concentrated sulfuric acid gives a lemon-yellow color. The addition of nitric acid (potassium nitrate) to the sulfuric acid solution gives a color change from greenish blue to violet to red and finally to yellow.

IMPURITIES.—1. **Colchiceine** ($C_{21}H_{23}O_6N.\frac{1}{2}H_2O$) is formed from colchicine as the result of hydrolysis, especially when the drug is extracted with acid media, but may readily be converted back into colchicine by esterification with methyl alcohol. Colchicine is the methyl ester of colchiceine. If 2 drops of ferric chloride solution are added to 5 cc. of a 1 per cent aqueous solution of colchicine, no color is produced in the mixture (*colchiceine*) but upon heating, the mixture develops a brownish red changing to brownish black.

2. **Chloroform-colchicine** is a crystalline combination ($C_{22}H_{25}O_6N.2CHCl_3$). When a mixture of 0.01 gm. of colchicine and 2 cc. of sodium hydroxide solution is heated and a drop of aniline added, no odor of phenylisocyanide is developed in the mixture (*chloroform*).

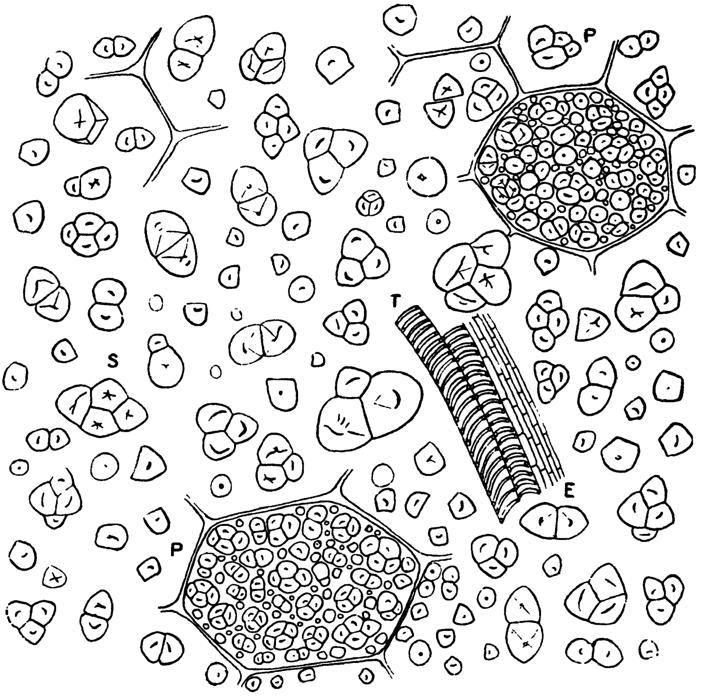


FIG. 58.—Powdered Colchicum Corm. Light brown or grayish brown fragments of thin-walled parenchyma (*P*) containing starch; starch grains (*S*) numerous, single or 2- to 6-compound, the individual grains varying from spheroidal or ovoid to polygonal, from 3 to 30 microns in diameter, and marked with a triangular or star-shaped, central cleft; tracheæ (*T*), few and with spiral or scalariform thickenings, occasionally accompanied by sieve (*E*); occasional fragments of epidermal cells with thick, reddish brown walls.

USES AND DOSE.—Colchicine is used for the same purposes as colchicum corm and seed. In combination with methyl salicylate, colchicine is believed to be superior to the crude drug for the treatment of gout. Dose, 0.5 mg. *Colchicine is extremely poisonous.*

The use of colchicine as a means of doubling chromosomes has opened a large field in plant genetics. Any numerical change in chromosome number entails a mutation which becomes evident in a number of the characteristics of the experimental plant. New species of plants of economic and pharmacognostic value may result from further research. The inter-relationship between the action of colchicine and mitosis is being investigated in animals; preliminary experiments show that injections of colchicine may be capable of effecting the dispersal of tumors.

Erythronium or Yellow Adder's Tongue (U. S. P. 1820 to 1863) consists of the root and herb of *Erythronium americanum* and is used like colchicum. In large doses it is emetic.

ALOE

Barbadoes or Curacao Aloe	*U. S. P.*
Aloe vulgaris Lamarck	1820 to 1882
Aloe vera Linné	1894 to date
Aloe chinensis Baker	1905 to 1916
Aloe barbadensis Miller	1942 to date
Cape Aloe	
Aloe spicata Baker	1851 to 1882, 1942 to date
Aloe ferox Lamarck	1916 to 1936, 1942 to date
Aloe africana Miller	1942 to date
Socotrine Aloe	
Aloe spicata Linné	1820 to 1851
Aloe socotrina Lamarck	1851 to 1894
Aloe Perryi Baker	1894 to date

Aloe, or Aloes (U. S. P. 1820 to date) is the dried juice of the leaves of *Aloe Perryi* Baker, known in commerce as Socotrine Aloe; or of *Aloe barbadensis* Miller (*Aloe vera* Linné), known in commerce as Curaçao Aloe; or of *Aloe ferox* Miller and hybrids of this species with *Aloe africana* Miller and *Aloe spicata* Baker, known in commerce as Cape Aloe.

Aloe is from the Arabic word *alloeh* or the Hebrew *halal*, meaning a shining, bitter substance; *vera* is from the Latin *verus*, meaning true, and *Perryi* is in honor of Wykeham Perry who made extensive studies on the plant. *Barbadensis* refers to the Barbadoes Islands; *ferox* is from the Latin meaning wild or ferocious; *africana* refers to the habitat of the plant, southern Africa; and *spicata* refers to the flowers in spikes.

There are about 150 species of *Aloe* known, most of which are indigenous to Africa. Many have been introduced into the West Indies and Europe. The aloes are typical xerophytic plants with fleshy leaves, usually having spines at the margin, and resemble to some extent the agave or century plant (*Agave americana*, Fam. *Amaryllidaceæ*).

Aloe Perryi grows on the Island of Socotra, in East Africa, and in Arabia. The plant is a perennial herb having a stem about 25 cm. long and 5 cm. in diameter surmounted by a rosette of about 20 leaves from 30 to 40 cm. long and from 5 to 7 cm. in diameter at the base. The leaves are cut and the juice from the cut end is allowed to drip into goats' skins where it evaporates spontaneously. The rather damp soft product is purchased by Arab traders in Socotra, and along the Red Sea and Zanzibar coasts and conveyed to Bombay where it is further dried and from where it is exported in kegs or tins. It is said that Socotrine aloe was known to the Greeks as early as the fourth century B.C. Alexander the Great sent a commission to the Island of Socotra to investigate the cultivation of the drug in 333 B.C. It was probably introduced into western Europe about the tenth century by the Arabs.

Aloe vera has a stem about 50 cm. high, the leaves being up to 50 cm. long, flat on one surface and convex on the other and having the spines arranged perpendicularly on the margin. It is a native of northern Africa but was introduced into the Barbadoes Islands in the seventeenth century. *A. chinensis*, a variety of *A. vera*, was introduced into Curaçao from China in 1817. The drug was cultivated to a considerable extent in Barbadoes until the middle of the nineteenth century, but since that time the industry seems to have died out. Curaçao aloe which is still often called Barbadoes aloe comes from the Dutch Islands of Curaçao, Aruba and Bonaire. The leaves are cut in March and April and placed cut-end downward in a V-shaped trough, the latter being inclined so that the juice may be led into a vessel. The juice is evaporated in a copper kettle and when of the proper consistency is poured into boxes or gourds and allowed to harden.

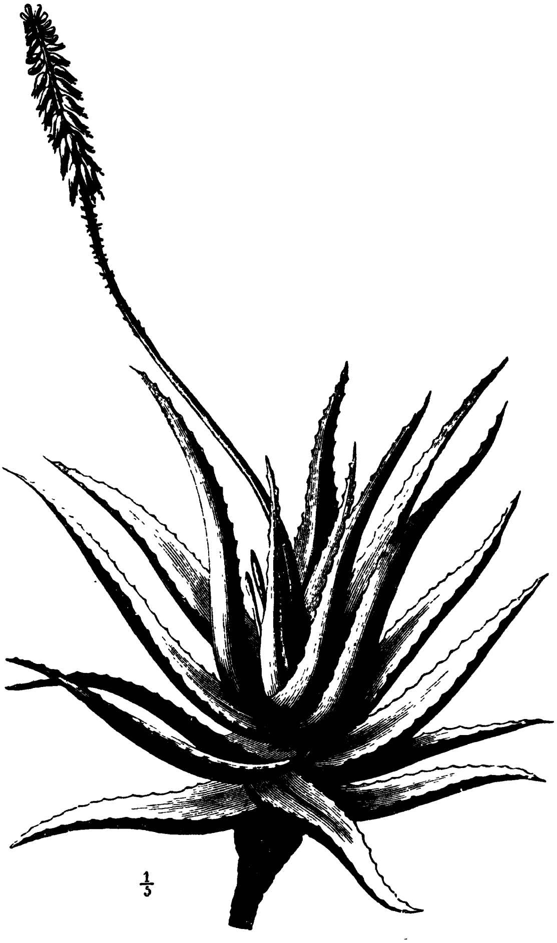


FIG. 59.—*Aloe vera*, the plant yielding Barbadoes aloe. Showing crown of thick, succulent leaves and the long spike (inflorescence) with the flowers on the upper portion of the axis. (After Engler.)

Cape Aloe is exported from Cape Colony and is largely used in veterinary practice.

DESCRIPTION AND POWDER.—See the U. S. Pharmacopœia. When powdered aloe is mounted in water the fragments tend to dissolve, leaving, however, a granular, insoluble residue. Glycerin mounts of Socotrine aloe show minute crystals of aloin embedded in the fragments.

CONSTITUENTS.—Aloe contains aloin (barbaloin), 5 to 30 per cent; a pale yellow volatile oil; resinous material 16 to 63 per cent; ash 1 to 4 per cent; moisture 10 to 20 per cent.

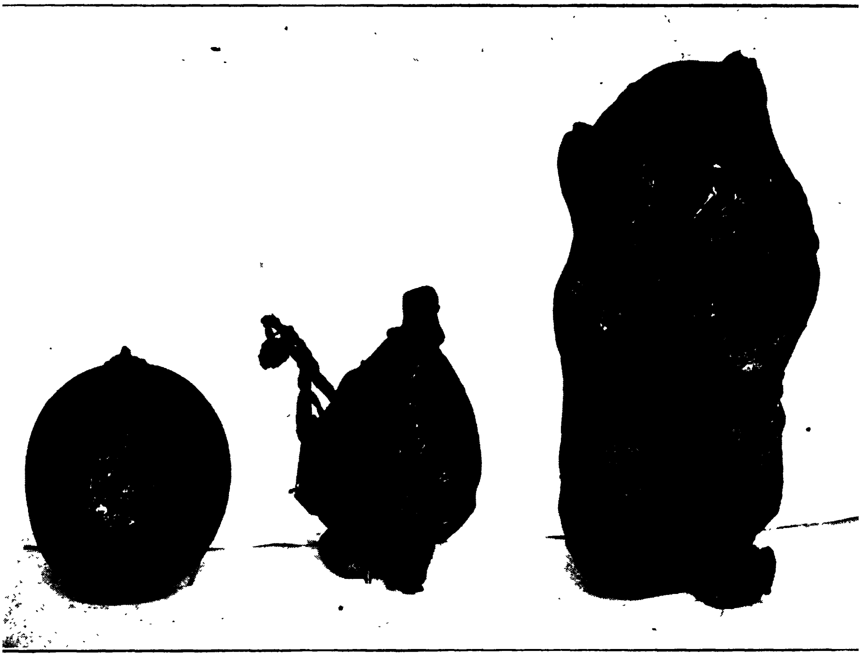


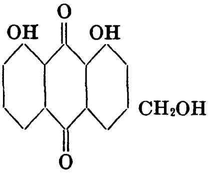
FIG. 60.—Special containers used in the shipment of aloes. The one on the left is a gourd and is still commonly used; the other two are sewed-up monkey skins which are now only occasionally seen in the market.

Aloin (U. S. P. 1894 to date; as a reagent, U. S. P. 1916 to 1926; N. F. 1926 to 1936) is a mixture of active principles obtained from aloe. It varies in chemical composition and in physical and chemical properties according to the variety of aloe from which it is obtained. Curaçao aloe yields the highest percentage of aloin (barbaloin) and it is the usual commercial aloin.

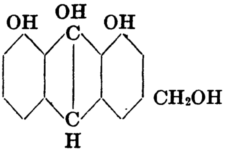
PREPARATION.—Dissolve aloe in 10 parts of boiling water; acidulate with sulfuric acid; cool to precipitate resin; filter and evaporate *in vacuo* to about 2 parts; seed with a crystal of aloin and allow to crystallize; wash the separated crystals with water and recrystallize from dilute alcohol. The yield varies from 4 to 30 per cent, from the different kinds of aloe.

PROPERTIES.—Aloin is a lemon-yellow to dark yellow microcrystalline powder, with a slight odor of aloe and an intensely bitter taste. It is readily soluble in water (not more than 1.5 per cent of insoluble residue in cold water); and easily decomposed in acid, and especially so in alkaline solutions. It yields not more than 0.6 per cent of ash.

Barbaloin is an anthraquinone glycoside and yields upon hydrolysis, *d*-arabinose, aloe-emodin and a reduction product, the anthranol of aloe-emodin (see Anthraquinone Derivatives, page 312).



Aloe-emodin



Aloe-emodinanthranol

Curaçao aloe contains a characteristic, crystalline isobarbaloin; Cape aloe an amorphous *b*-barbaloin, also present to some extent in Socotrine aloe, but is said to be absent from Curaçao. Aloe contains enough free anthraquinones to give the Bornträger test. The aloe resins consist of resinotannols combined with cinnamic or *p*-hydroxycinnamic (*p*-coumaric) acids.

Standards.—Aloe yields not more than 4 per cent of ash, not more than 12 per cent of moisture, and not less than 50 per cent of water-soluble extractive.

Tests.—Prepare a solution by macerating 1 gm. of powdered aloe in 100 cc. of water for two hours with frequent agitation; filter and use the filtrate for the following tests.

1. **Schönteten's Reaction.**—Mix 5 cc. of the filtrate with 45 cc. of water and add 20 cc. of a solution of sodium borate (1 in 20) to the mixture. A greenish fluorescence is developed which gradually disappears, the mixture becoming brownish on standing. The greenish fluorescence was formerly supposed to be due to barbaloin but is now definitely known to be due to the aloe-emodin anthranol. All varieties of aloe give the reaction.

2. **Bornträger's Test.**—Dilute 10 cc. of the filtrate to 100 cc. with water and shake the dilution with 10 cc. of benzene. Separate the benzene layer and shake it with 5 cc. of ammonia T.S.: a deep rose color is produced in the lower layer. This test is commonly applied to all anthraquinone drugs (see page 348) and is due, in this case to aloe-emodin which is present to some extent in the free state in all varieties of aloe (except Natal aloe).

3. **Color.**—When viewed in the bulb of a volumetric flask the filtrate from Socotrine aloe is dark yellow, from Curaçao aloe dark orange, and from Cape aloe greenish yellow.

4. **Nitric Acid Reactions.**—Add 2 cc. of nitric acid to 5 cc. of the filtrate. Socotrine aloe gives a yellow color, Curaçao aloe a deep red color, and Cape aloe a reddish brown color changing to vivid green. Nitric acid may be applied directly to the powdered drugs with somewhat similar results.

5. **Cupraloin Test.**—Mix 5 cc. of the filtrate with 5 cc. of water; add a drop of 10 per cent copper sulfate solution, about 0.5 gm. of sodium chloride and 1 cc. of alcohol and warm gently. With Curaçao aloe the color changes to reddish violet and remains permanent. The test is a specific one for isobarbaloin and therefore is an identity test for Curaçao aloe. Socotrine aloe gives no reddish violet color and Cape aloe gives a transient pink (Cape aloe contains traces of isobarbaloin).

6. **Nitrous Acid Test.**—Add a few crystals of sodium nitrite to 5 cc. of the filtrate and follow with a drop of glacial acetic acid and shake. In the presence of Curaçao aloe the mixture turns a distinct and permanent carmine red. With Cape aloe the color is pinkish. Socotrine aloe gives no distinct color. This test is again a specific test for isobarbaloin and the varieties of aloe containing it.

Uses and Dose.—Aloe is a cathartic, acting mostly on the large intestine. It is also an emmenagogue and a vermifuge. Average dose, 0.25 gm.; of aloin, 15 mg.

Adulterants.—Aloe has been found adulterated with gums, dirt and various mechanical impurities and with drugs from which the aloin has been removed. One commercial variety is frequently substituted for another more expensive one. The absence of gum or inorganic impurities is indicated by a nearly clear solution after gentle heating and then cooling a 2 per cent solution of aloe in alcohol.

Allied Products.—Several other commercial varieties of aloe are found on the market among which the following might be named:

Zanzibar Aloe is probably a "hepatic" variety of Socotrine aloe. It is usually packed in small animal skins and shipped from the eastern African coast through Bombay. It responds to the tests indicating Socotrine aloe.

"Hepatic" refers to the opaque, liver-colored types of aloe made by slow evaporation of the juice which permits minute crystallization in the mass. "Vitreous" or "glassy" aloes, made by rapid evaporation, show no imbedded crystals, hence in thin layers are translucent, bright and shiny.

Uganda Aloe is the hepatic variety of Cape aloe.

Natal Aloe is a hepatic variety of aloe which was at one time exported from Natal, the botanical origin being unknown. It resembles Cape aloe, but the powder dissolved in nitric acid assumes a permanent crimson color; dissolved in sulfuric acid and vapor of nitric acid produces a deep blue color; these tests distinguish it from other varieties of aloe. It contains nataloin but not emodin. It is less active medicinally than other aloes.

Jaffarabad Aloe is a vitreous variety obtained from the East Indies and is exported from Bombay. It yields 13 to 20 per cent of aloin, which is apparently chiefly barbaloin, and gives a deep crimson with nitric acid.

Aloe Leaf, fresh, or the pulp of fresh aloe leaves, particularly *Aloe barbadensis*, have been used to increase the rate of healing of acute *X*-ray burns.

SQUILL

Squill, Scilla bulbus P. I. (U. S. P. 1820 to 1942; N. F. 1942 to date) consists of the cut and dried fleshy inner scale of the bulb of the white variety of *Urginea maritima* (Linné) Baker, known in commerce as White or Mediterranean Squill; or of *Urginea indica* Kunth, known in commerce as Indian Squill.

Scilla is from the Greek *skilla,* meaning to split (referring to the separating scales); *Urginea* may be from the Latin *urgere,* meaning to press and referring to the compressed seed; *maritima* is from the Latin and refers to the habitat of the plant on the Mediterranean coasts of Spain, France, Italy, Greece, Algiers and Morocco. The bulbs, which grow half immersed in the sandy soil near the sea, are gathered late in August and after removal of the membranous outer scales and the central portion, the fleshy scales are cut into transverse pieces and dried. Squill was known to the Egyptians and to the Greeks. Dioscorides mentions a vinegar of squills, and an oxymel of squill was used by Arabian physicians.

Description and Histology.—See Figure 61 and the National Formulary.

Powder.—Yellowish white to very pale brown, with a slight odor and a mucilaginous, bitter and acrid taste. It has a tendency to form a hard cake unless kept in a dry atmosphere. The characteristic crystals of calcium oxalate are the longest in any drug and alone serve to identify it; the spiral or reticulate tracheæ are few, starch grains are rare, and only occasional stomata are found.

Constituents.—Scillaren-A is crystalline, sparingly soluble and comprises about two-thirds of the total glycosidal content. Upon hydrolysis it yields scillaridin-A and a disaccharide, which is convertible into glucose and rhamnose. Scillaren-B is amorphous, easily soluble in water and upon hydrolysis, yields scillaridin-B; the older terms scillipicrin, scillitin and scillitoxin represent mixtures of the above glycosides, or impure substances. Squill contains also a little volatile oil; about 22 per cent of sugar; considerable calcium oxalate; and a mucilage, sinistrin, which yields levulose on hydrolysis and gives, with Tunman's reagent, an inulin-like reaction.

STANDARDS.—Squill, as fluidextract, possesses a potency per cubic centimeter equivalent to not less than 0.8 mg. and not more than 0.9 mg. of standard ouabain.

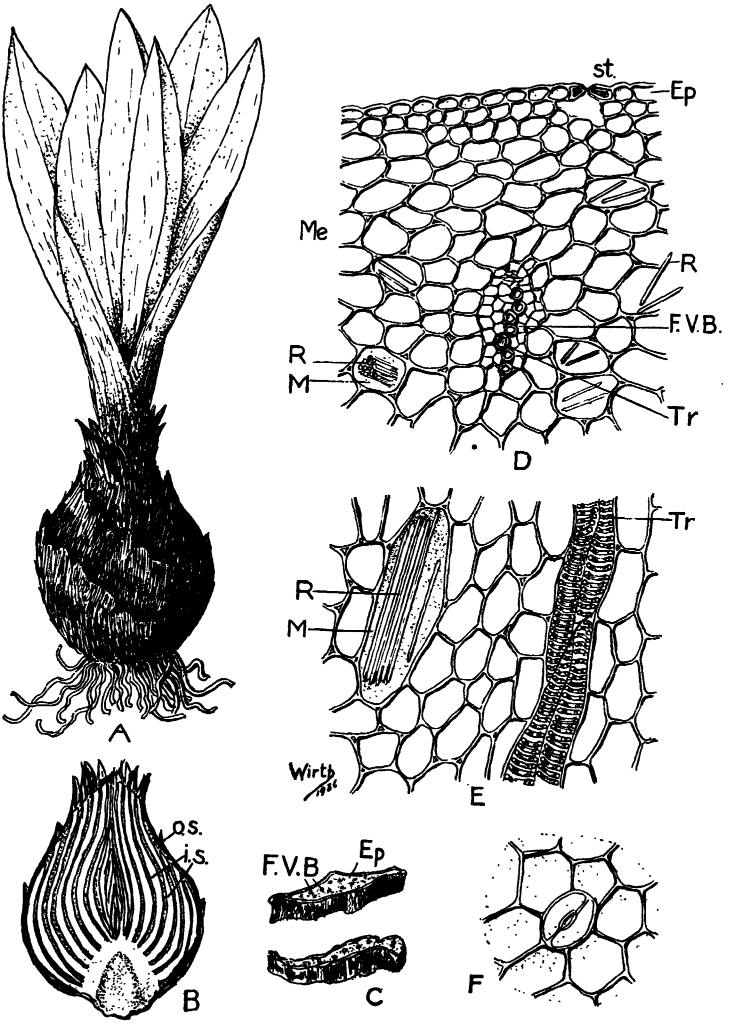


FIG. 61.—*Urginea maritima.* *A*, entire plant in the leaf stage showing bulb with outer coriaceous scales. *B*, longtitudinal section through a squill bulb showing outer (*os*) and inner scales (*is*). *C*, cut fragments of the scales which constitute the drug. These occur in irregularly curved or flattened pieces (0.5 to 5 cm. long) which are weak yellowish orange or pale yellow in color, the cut surface showing slightly raised vascular bundles (*FVB*). The drug has a slight odor and a mucilaginous, bitter and acrid taste. *D*, transverse section of the outer portion of a scale showing thin-walled epidermis (*Ep*) with occasional stomata (*st*); mesophyll (*Me*) composed of parenchyma, an occasional vascular bundle (*FVB*) with spiral tracheæ (*Tr*), and frequent longitudinally elongated cells containing mucilage (*M*), embedded in which are bundles of calcium oxalate raphides (*R*) up to 1000 microns in length. *E*, longitudinal section through a scale. *F*, surface view of the epidermis showing a stoma. (Drawing by Wirth.)

Uses and Dose.—Squill is an expectorant, an emetic, a cardiac stimulant and a diuretic. Average dose, 100 mg. Scillaren, a mixture of the glycosides of squill in natural proportions, and Scillaren-B possess a cardiac action similar to that of digitalis, though the action may not be as persistent. The oral dose of scillaren is 1.6 mg. three to four times daily; the intravenous dose of scillaren-B is not more than 0.5 mg. during twenty-four hours.

Adulterants and Substitutes.—Squill has been adulterated with stones resembling the drug in size and color. The bulbs of several species of *Crinum* (Fam. *Amaryllidaceæ*) found growing in Brazil, China, southern Asia and the East Indies have been used as substitutes for squill.

Red Squill consists of the bulb or bulb scales of the red variety of *Urginea maritima*, which is imported to a considerable extent for use as a rat poison. It should not be present in the official squill and may be detected by the presence of red, pink or purple epidermal or parenchyma tissues.

Allium or Garlic (U. S. P. 1820 to 1905; N. F. 1916 to 1936) is the fresh bulb of *Allium sativum* Linné. It is a native of southern Europe and is extensively cultivated, being considerably employed as a condiment. The bulb is subglobular, 4 to 6 cm. broad, compound, consisting of 8 to 15 bulbels and surrounded by 1 or 2 dry, whitish, membranous scales and attached to a flattened circular base, from the lower portion of which arise numerous yellowish white roots; odor aromatic, disagreeable; taste intensely pungent and persistent.

Garlic contains about 0.25 per cent of a yellowish volatile oil containing sulfur compounds and having a strong unpleasant odor. It is a carminative, an expectorant and a diuretic, the average dose being 2 gm.

CONVALLARIA

Convallaria Root or Lily-of-the-valley Root (U. S. P. 1882 to 1916; N. F. 1916 to date) consists of the dried rhizome and roots of *Convallaria majalis* Linné.

Convallaria Flowers or Lily-of-the-valley Flowers (N. F. 1916 to 1926) is the dried inflorescence of *Convallaria majalis* Linné, without the presence of more than 5 per cent of foreign matter.

Convallaria is from the Latin *convallis*, meaning growing in valleys, and *leiron*, meaning lily; *majalis* signifies blooming in May. The plant is a low-growing perennial herb indigenous to Europe, Asia and the mountains of southeastern United States, and is extensively cultivated for its flowers.

The flower is collected in the spring and the rhizome and roots in late summer. Both are carefully and promptly dried. Convallaria has been used as a domestic remedy for centuries, and entered into general medical practice about 1850. It has never attained the reputation of digitalis. The relative potency between Convallaria herb, flowers and rhizome-roots is the ratio 6:10:85.

Description, Histology and Powder.—Of Convallaria Root, see Figure 62 and the National Formulary. The flower drug consists of racemes of white flowers (brownish when dried) on long greenish flower stalks; the perianth is bell-shaped, 6-parted, recurved; stamens 6, and ovary 3-locular. The odor is fragrant and the taste sweet and acrid.

Constituents.—In Convallaria Root: convallamarin, a bitter, crystalline glycoside, about 0.6 per cent, which is soluble in water, alcohol and ether and has a physiological action similar to digitalin; an acrid glycoside, convallarin, insoluble in ether and sparingly soluble in water, the solution foaming like that of a saponin; and convallatoxin, occurring in needle-like crystals only slightly soluble in water. The flower drug probably contains the active constituents mentioned above as well as a volatile crystalline principle which is very fragrant.

STANDARDS.—Convallaria Root, when tested by the official method, possesses

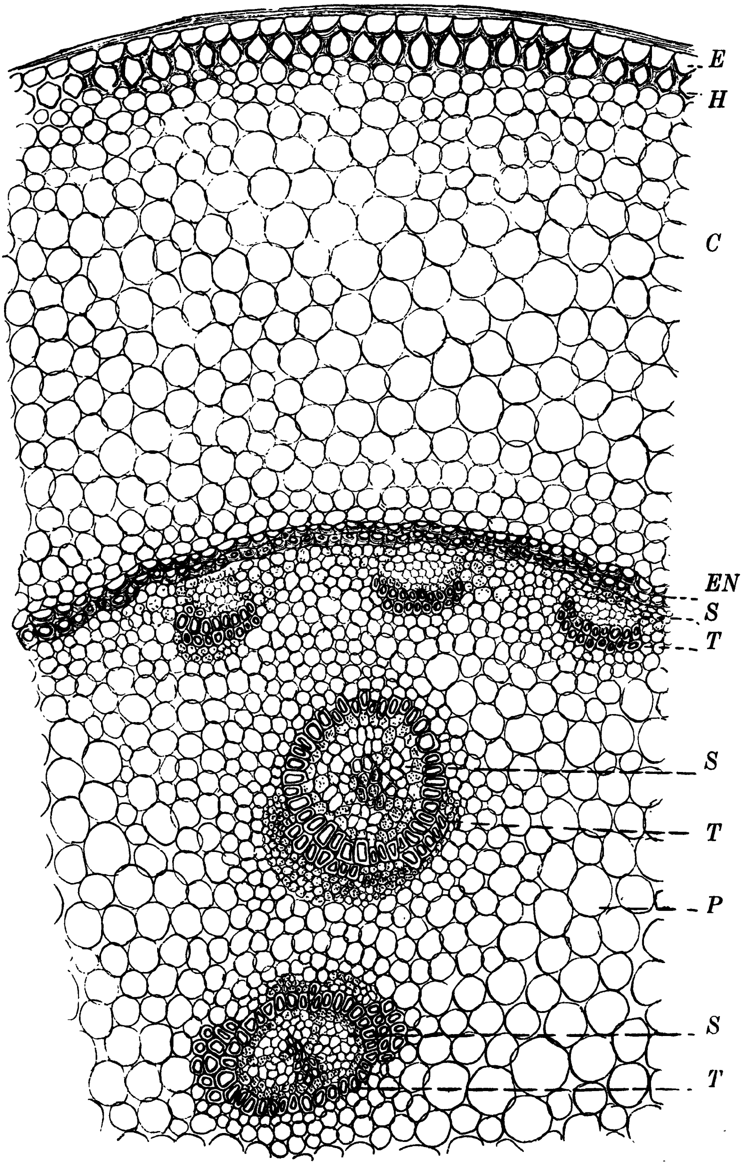


FIG. 62.—Convallaria Rhizome: *E*, epidermis bearing a thick layer of cutin; *H*, hypodermis of collenchyma; *C*, cortex of about 20 rows of parenchyma, bearing starch and calcium oxalate; *EN*, endodermis with cells which have the radial and inner walls thickened and adjacent to which lie U-shaped closed collateral bundles; *S*, sieve; *T*, tracheæ and fibers; *P*, parenchyma.

a potency such that 0.1 gm. of it is equivalent to 3 U. S. P. digitalis units. It contains not more than 5 per cent of leaves or other foreign organic matter and yields not more than 6 per cent of acid-insoluble ash.

Uses and Dose.—Convallaria is a heart tonic and a diuretic. Average dose of Convallaria Root 30 mg.; of the flower drug 500 mg.

Polygonatum or Solomon's Seal, the rhizome and roots of *Polygonatum commutatum,* contains convallarin, asparagin, mucilage and starch.

SARSAPARILLA

	U. S. P.
Honduras	
Smilax Sarsaparilla	1820 to 1842
Smilax officinalis Kunth	1842 to 1942
Smilax Regelii Killip and Morton	1942 to date
Mexican	
Smilax medica Chamisso and Schlechtendal	1882 to 1942
Smilax aristolochiæfolia Miller	1942 to date
Para	
Smilax papyracea Duhamel	1894 to 1916
Jamaica	
Smilax ornata Hooker	1905 to 1942
Ecuadorian	
Associated with Honduras	1942 to 1947
Undetermined species of Smilax	1947 to date
Central American	
Associated with Jamaica	1926 to 1942
Undetermined species of Smilax	1942 to date

Sarsaparilla (U. S. P. 1820 to date) is the dried root of *Smilax aristolochiæfolia* Miller, known in commerce as Mexican Sarsaparilla; or of *Smilax Regelii* Killip and Morton, known in commerce as Honduras Sarsaparilla; or of undetermined species of *Smilax* respectively known in commerce as Ecuadorian and Central American Sarsaparilla.

The name Sarsaparilla is from the Spanish *zarza,* a bramble, *parra,* a vine, and *illa,* small—a small brambly vine. *Smilax* is the Greek name for the yew and several other plants; *officinalis* means a workshop and alludes to the use of the root in the drug shop; *medica* refers to the medicinal qualities; and *ornata* to the ornamental character of the species; *aristolochiæfolia* refers to the leaves similar to those of several aristolochia species; and *Regelii* is in reference to the botanist Dr. Edward Regel, who has done much work on these *Smilax* species.

The plants are climbing or trailing vines with prickly stems, usually growing in damp soil. The roots are dug (sometimes with the rhizome) and dried in the sun. The rhizomes are short, thick and knotty; the roots are very long, roughly furrowed and quite uniform in thickness, seldom exceeding 6 mm. in diameter. The masses of roots are loosely bundled or tightly rolled and bound into cylinders according to the commercial kinds.

Description, Histology and Powder.—See Figures 65, 66, 67 and the U. S. Pharmacopœia.

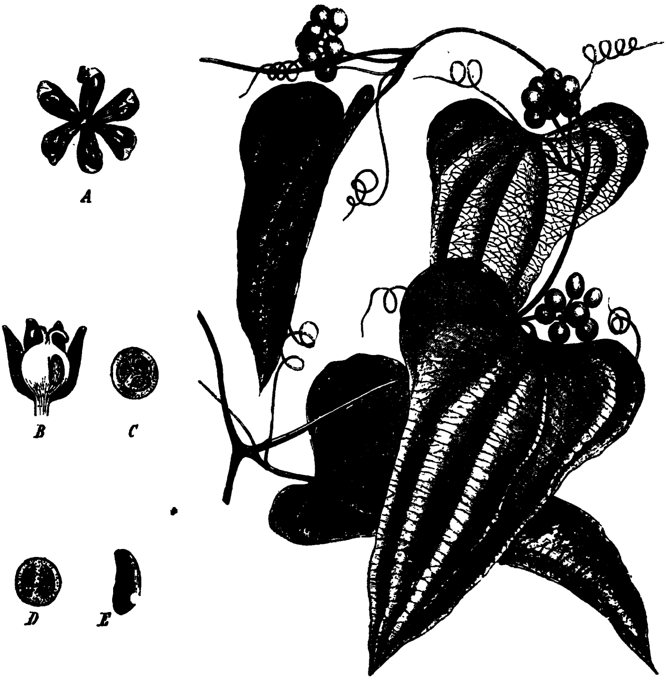


Fig. 63.—*Smilax aristolochiæfolia* yielding Mexican sarsaparilla. To the right a portion of branch showing the characteristically veined leaves, the tendril-like appendages on the petioles, and the axillary, umbel-like clusters of fruits. *A*, staminate flower; *B*, pistillate flower in longitudinal section; *C*, transverse section of the tri-locular ovary; *D*, longitudinal section of ovary; *E*, seed. (After Bentley and Trimen.)

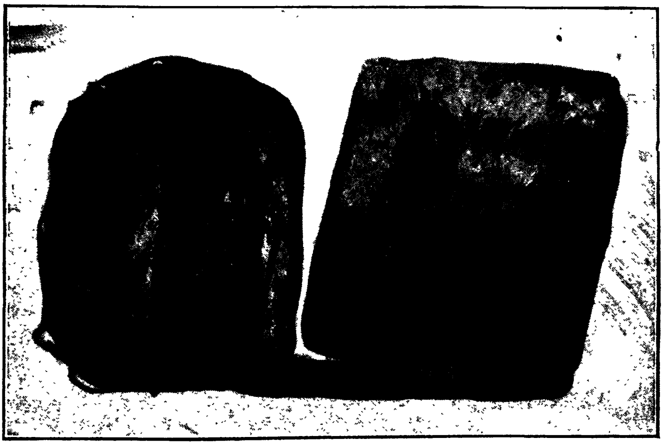


Fig. 64.—"Ceroons" made of hide, in which Honduras sarsaparilla is imported

Constituents.—Power and Salway succeeded in isolating sitosterol-*d*-glycoside (phytosterolin), sitosterol, stigmasterol, a new crystalline sarsapic acid and a crystalline glycoside, sarsasaponin. Parillin and smilacin, which have been reported as glycosides, have been shown, by them, to be impure forms of sarsasaponin. Sarsaparilla also contains considerable starch and calcium oxalate.

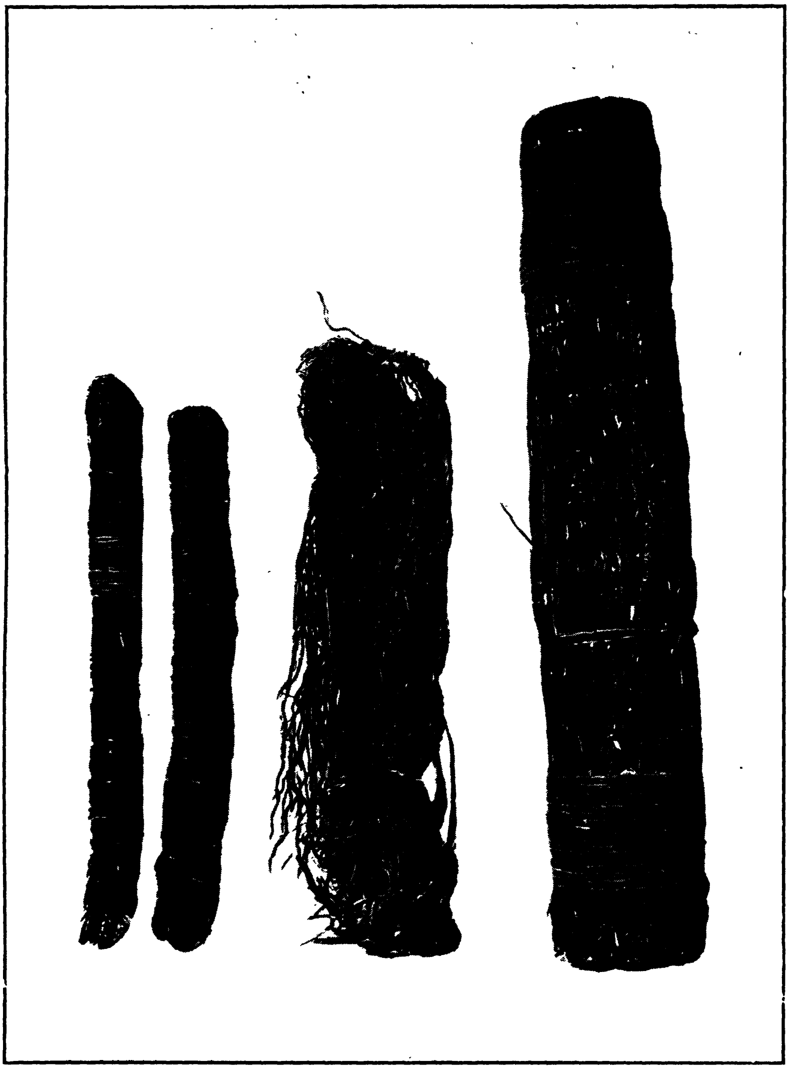


Fig. 65.—Bundles of sarsaparilla, the two on the left being Honduras; the next one, Mexican, and the large one, Para, which is, however, not an article of commerce at the present time. (About ⅛ natural size.)

Standards.—Sarsaparilla contains not more than 2 per cent of foreign organic matter, other than the rhizome and crown portion. Mexican and Ecuadorian sarsaparilla contain not more than 10 per cent of rhizome and

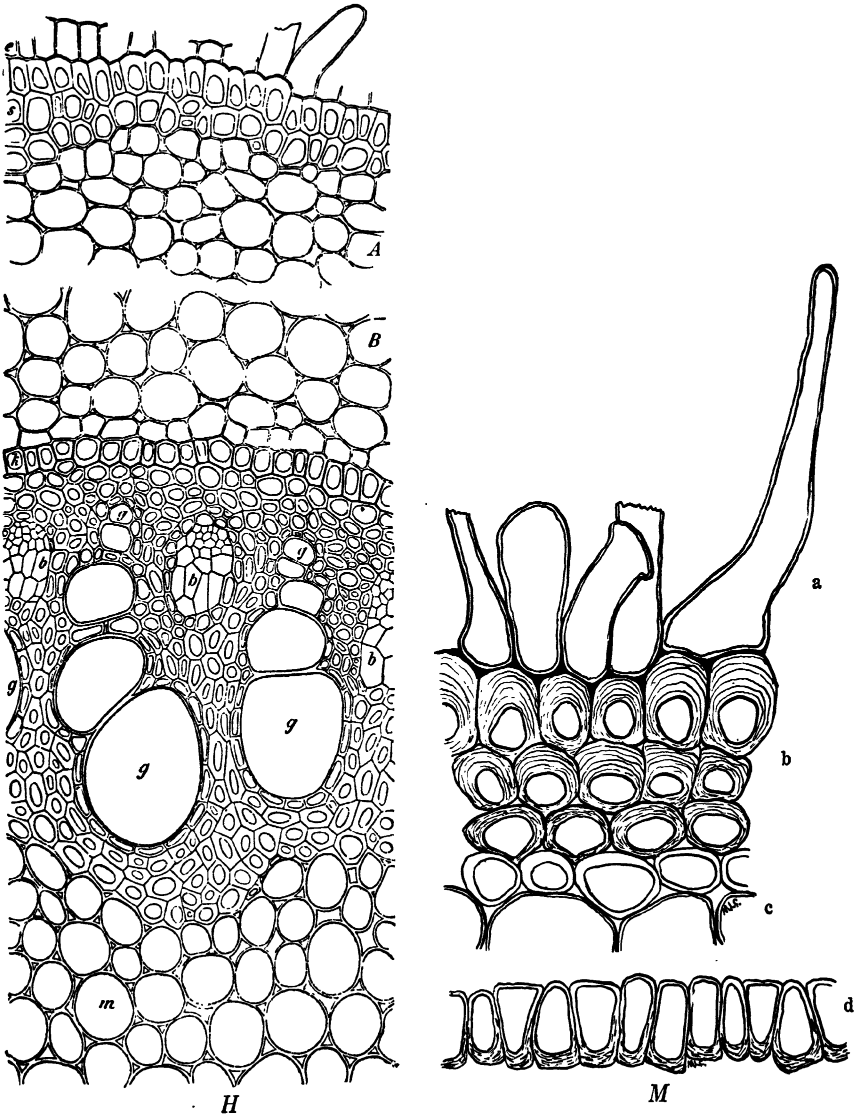


Fig. 66.—*H*, transverse section of Honduras sarsaparilla in which the middle portion of the cortex is omitted: *e*, epidermis with root hairs; *s*, hypodermis of two rows of cells with thickened, relatively uniform walls; *A*, outer portion of cortex and *B*, inner portion of cortex, with cells containing starch, resin or raphides of calcium oxalate; *k*, endodermis of nearly square cells with uniformly thickened walls; *g*, tracheæ; *b*, sieve cells; *m*, parenchyma of the pith, the cells resembling those of the cortex. The thick-walled cells around the tracheæ (*g*) and phloem (*b*) are sclerenchyma fibers. (After Luerssen.) *M*, Mexican sarsaparilla in transverse section; epidermis (*a*) of radially elongated cells (root-hairs); hypodermis (*b*) of three or more rows of cells with the outer walls more thickened than the inner; parenchyma cells (*c*); and endodermis (*d*) of radially elongated cells with the inner walls more thickened than the outer. The walls of hypodermal and endodermal cells are slightly lignified dna with an outer lamella of suberin. (Drawing by M. C. Day.)

stem, and Mexican sarsaparilla yields not more than 4 per cent of acid-insoluble ash. The other official sarsaparillas yield not more than 2 per cent of acid-insoluble ash.

USES AND DOSE.—Sarsaparilla is a tonic and an alterative. Average dose, 2 gm.

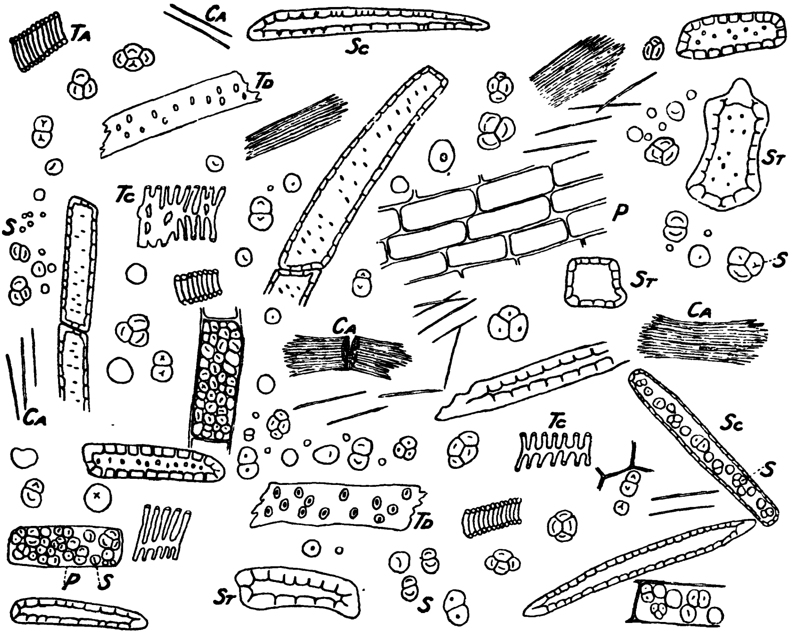


FIG. 67.—Powdered Sarsaparilla: consisting mostly of starch-bearing parenchyma (*P*) and separate starch grains (*S*), the latter from 3 to 23 microns in diameter, spheroidal, or biconvex or spheroidal-tetrahedral, single, or 2- to 4-compound, and frequently with a central elliptical cleft; calcium oxalate in raphides (*Ca*), attaining a length of 150 microns, occurring singly or in groups; cells of the hypodermis and endodermis with lemon-yellow or reddish yellow porous walls and, in the case of Mexican sarsaparilla, showing an uneven or irregular thickening, the individual cells, 80 to 500 microns in length; fragments of tracheæ with simple and bordered pores (*Td*), scalariform, reticulate (*Tc*), or spiral (*Ta*) thickenings, and associated with selerenchymatous fibers (*Sc*) having rather thin, slightly lignified and porous walls; occasional stone cells (*St*) from the stem-bases or "butts." (Drawing by Hogstad.)

Aralia Nudicalis, Aralia Racemosa and Aralia Spinosa (see pages 456 to 458) have been used medicinally as alteratives and tonics. Aralia Nudicalis is commonly known as American or False Sarsaparilla. The roots of *Cocculus villosus* are used in the East Indies like Sarsaparilla.

China Root is used to some extent in Europe. It consists of the tuberous roots of an eastern Asiatic species of *Smilax*. **Indian Sarsaparilla** is derived from *Hemidesmus indicus* (Fam. *Asclepiadaceæ*). **Para Sarsaparilla** (U. S. P. 1894 to 1916), from *Smilax papyracea*, was formerly imported from South America but is now apparently entirely off the market (see Fig. 65).

Aletris, Star Grass or Unicorn Root (U. S. P. 1820 to 1873; N. F. 1916 to 1947) consists of the dried rhizome and roots of *Aletris farinosa* Linné. The plant is a perennial herb with spreading lanceolate leaves crowded at the base and a long slender scape terminated by a raceme of small, white, tubular flowers. It is common in the pine barrens and grows in grassy woods throughout the eastern United States. Commercial supplies come largely from North Carolina, Virginia and Tennessee.

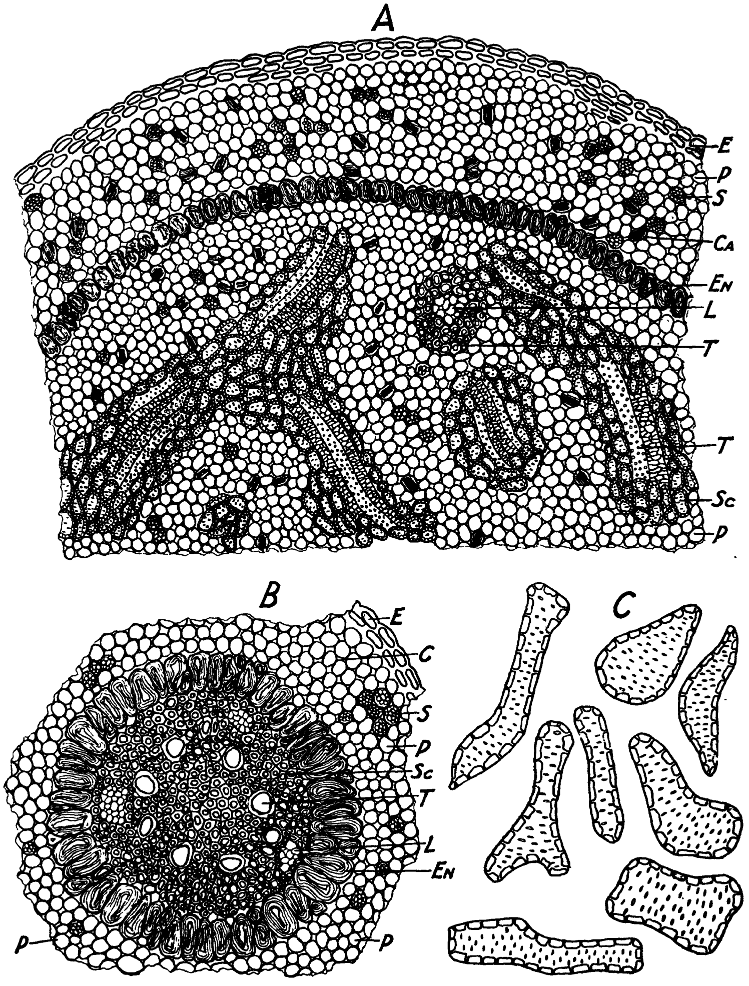


FIG. 68.—*Aletris.* *A*, transverse section of rhizome showing epidermis (*E*); cortical parenchyma containing either starch grains (*S*) from 2 to 10 microns in diameter or raphides of calcium oxalate (*Ca*) from 15 to 35 microns in length; endodermis (*En*) more or less distinct in the living plant but usually not well marked in the drug; fibrovascular bundles composed of tracheæ (*T*) and sieve (*L*); sclerenchymatous fibers (*Sc*). *B*, transverse section of root showing epidermis (*E*); cortical parenchyma containing starch (*S*); endodermis (*En*) consisting of thick-walled reddish fibers; tracheæ (*T*); sclerenchymatous fibers (*Sc*); sieve (*L*). *C*, isolated, porous sclerenchymatous cells from the rhizome. (Drawn by Haase.)

Rhizome horizontal or slightly oblique, somewhat contorted, from 2 to 4 cm. in length, 5 to 12 mm. in diameter; externally grayish brown; upper portion with circular stem scars and numerous leaf bases, the sides and lower portion with numerous pale yellow roots, from which the cortical layer is often stripped, exposing the reddish brown endodermal layer of the stele and giving them a wiry appearance; fracture short; internally light brown; odor slight, acetous; taste sweetish, somewhat bitter.

The structure is well shown in Figure 68. The drug contains a bitter principle and is used as a uterine tonic and a diuretic. Average dose, 2 gm.

Helonias, Blazing Star or False Unicorn (N. F. 1916 to 1947) consists of the dried rhizome and roots of *Chamælirium luteum* (Linné) Asa Gray. The plant is a perennial, dioecious herb having a rather fleshy bitter rhizome, a number of basal leaves and an herbaceous slender stem from 3 to 5 dm. in length terminated by a spike-like raceme of small white flowers. It grows in moist meadows and thickets throughout the eastern United States.

The rhizome is upright, or oblique, nearly cylindrical, from 0.5 to 3 cm. long, externally grayish brown, annulate from scars of bud-scales; upper portion with leaf-bases enclosing a small bud; lower portion with numerous whitish or pale yellowish, nearly straight wiry roots, free from the cortical layer, and numerous pits from which former roots once protruded; fracture hard and horny; internally, grayish yellow with cortex 3 to 4 mm. thick and central cylinder with 3 or 4 circles of small, nearly circular fibrovascular bundles.

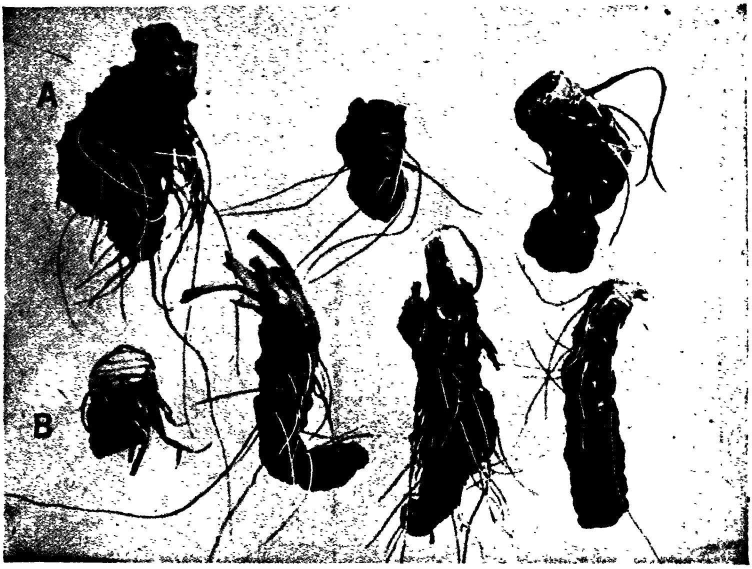


FIG. 69.—Several types of Helonias rhizome: *A*, oblique rhizome with stem-base and two stem-scars; *B*, upright rhizome showing new growth at top. (Moser.)

The powdered drug is light yellow, with a slight odor and a bitter, slightly astringent taste; numerous fragments of parenchyma, the cells containing starch grains which are spheroidal or ellipsoidal and up to 15 microns in diameter; bundles of calcium oxalate raphides from 25 to 40 microns in length; fragments of lignified cork tissue; numerous fragments of tracheæ associated with more or less lignified fibers.

Helonias contains a bitter glucoside, chamælirin, about 10 per cent, amorphous, soluble in water, the solution frothing like saponin solution; with dilute acids it forms a resinous body, chamæliretin, which is also soluble in water. The "Eclectic" extract known as helonin is a hydro-alcoholic extract of the drug and is a mixture of principles.

Helonias is a diuretic and uterine tonic. Average dose, 2 gm.

ADULTERANTS.—The rhizome of several species of *Liatris*, especially *L. spicata* (Fam. *Compositæ*) is said to have been substituted for Helonias. These rhizomes have an aromatic, somewhat terebinthinate odor and a bitter acrid taste. They contain 0.1 per cent of a volatile oil, 5 per cent of resin and 2 per cent of a caoutchouc.

Trillium or Bethroot (N. F. 1916 to 1947) consists of the dried rhizome and roots of *Trillium erectum* Linné or other species of *Trillium.*

The plant is a low perennial herb growing in rich woods from Canada to North Carolina, producing a rather stout stem, having three leaves arranged in a whorl at the summit and subtending the large, sessile, dark purple flowers which have an unpleasant odor. Trillium was used by American Indians in parturition from which the name "birthroot," contracted into "bethroot" has come into usage.

The rhizome is upright or oblique; up to 5 cm. in length and 3 cm. in width; nearly cylindrical and terminated above by a bud surrounded by the bases of the scarius bud-scales; annulated by scale scars; stem scars few; externally yellowish to reddish or dark brown; internally whitish or pale yellow; fracture somewhat uneven usually with a hard and waxy texture. Roots many, mostly brittle, 1 to 3 mm. in diameter, distinctly annulate and usually lighter in color than the rhizome.

The powdered drug is nearly white; odor distinct; taste bitter and acrid, producing a sialagogue effect; numerous, simple, spherical starch grains up to 20 microns in diameter, occasionally larger; raphides of calcium oxalate up to 60 microns long, occasionally much longer; tracheæ few, reticulate or spiral, rarely over 26 microns wide; fragments of thin-walled parenchyma, and of reddish brown epidermal and hypodermal cells with unevenly thickened walls.

Trillium contains a saponin (trillin) about 5 per cent, considerable starch, and a small quantity of volatile oil.

Trillium has been used as a uterine stimulant but is of questionable value. Average dose, 2 gm.

DIOSCOREACEÆ, OR YAM FAMILY

These are mostly twining plants with large tuberous roots or knotted rootstocks. There are about 175 species, most of which are indigenous to the West Indies and South America. The anatomy of the stems is interesting in that the fibrovascular bundles are collateral and arranged in a manner similar to those found in dicotyledons. In the rhizomes the fibrovascular bundles are of a collateral type but are separated from each other, as is usual in the monocotyledons.

Dioscorea or Wild Yam Root (N. F. 1916 to 1942) is the dried rhizome of *Dioscorea villosa* Linné.

The plant is an herbaceous twining perennial, with beautiful, cordate, 9- to 11-ribbed leaves, small greenish yellow flowers and triangular winged capsules. It is common in the eastern and central United States and is easily cultivated. Commercial supplies come largely from Virginia, North Carolina, Indiana and Michigan.

The rhizome is knotted and woody, elongated, 6 to 20 mm. thick, often compressed, bent and branched, bearing stem-scars on the upper surface, and scattered nodular projections or a few slender tough steles of the roots or thorn-like root remains in circular depressions below; externally pale brown, more or less scaly; fracture short but tough, the fractured surface whitish or pale yellowish, with numerous small, scattered, yellowish wood bundles.

The powdered drug is nearly white and odorless; taste starchy, insipid but becoming acrid. It contains numerous fragments of thick-walled, lignified parenchyma cells, many of which contain spherical or ovoid starch grains up to 35 microns in diameter; numerous isolated starch grains and a very few raphides of calcium oxalate; a few fragments of thin-walled parenchyma cells; fragments of fibrovascular bundles with tracheæ and tracheids, which have minute bordered pores; yellowish or brownish fragments of epidermal tissue; a few isolated lignified fibers.

The drug contains an acrid resin and a principle allied to saponin; total ash from 1.35 to 3 per cent, and acid-insoluble ash about 0.2 per cent. Continued boiling is said to impair the acrid properties of the drug.

Dioscorea is a diaphoretic and an expectorant. Average dose, 4 gm.

Allied Plants.—**Yam** is a popular name for several of the edible species of *Dioscorea* and is sometimes incorrectly applied to certain varieties of the sweet potato. The tubers of *D. alata* weigh as much as 25 kg. In the South Sea Islands they are eaten after boiling, which destroys the acrid principle. The starch is also separated and is sometimes marketed under the name of **South Sea Arrowroot.**

IRIDACEÆ, OR IRIS FAMILY

These plants are mostly perennial herbs with erect, bilateral leaves, and interesting, frequently handsome flowers. There are about 800 species, occurring in both temperate and tropical climates. Some have rhizomes (*Iris*) which are creeping and the fibrovascular bundles are of concentric type, being of the collateral type only as they enter the leaves; others, like *Crocus*, have a corm. Of special interest is the fact that the calcium oxalate occurs in the form of long styloids, which are surrounded with mucilage, and the walls of the cells in which they are enclosed are suberized.

Several of the genera (*Iris, Crocus, Gladiolus*) are widely cultivated for the beauty of their flowers.

CROCUS

Crocus or Spanish Saffron (U. S. P. 1820 to 1905; N. F. 1916 to 1942) is the dried stigma of *Crocus sativus* Linné.

The plant is a low-growing, perennial herb, producing its flowers in the autumn from buds on the large corm. The flowers are 25 mm. or more across, lily-like, and the three stigmas terminate a long style. The flowering period extends over two or three weeks, the flowers being gathered as they open; the dark red stigmas are separated by hand and are dried over charcoal fires, with a loss in weight of about 80 per cent. The stigmas from about 100,000 flowers are required to make a kilo of the pure dried drug, hence the price of the drug is very high.

The plant is indigenous to the eastern Mediterranean region and is cultivated for the drug in Spain, France, Austria, Germany, Switzerland and Persia. The imports to the United States are largely from Spain; that from Valencia consists mostly of stigmas only; that from Alicante is usually contaminated with styles, stamens and corolla fragments.

Saffron was known to the Egyptians and was prized by the ancient Greeks and Romans. Even in the middle ages it was an expensive drug. Saffron seems to have been introduced into Spain about the tenth century.

Description and Structure.—See Figure 70.

Crocus contains a yellow glycoside, crocin, of which 1 part in 100,000 parts of water forms a distinctly yellow solution; also another glycoside, picrocrocin, which hydrolyses to form a volatile oil, about 1 per cent of the dried drug, and which gives the characteristic odor to the drug; it also contains wax, fixed oil and dextrose.

Crocus meets the following standards:

1. Contains not more than 10 per cent of the yellow styles of the plant, or 2 per cent of other foreign organic matter.
2. Yields not more than 7.5 per cent of total ash, or 1 per cent of acid-insoluble ash.

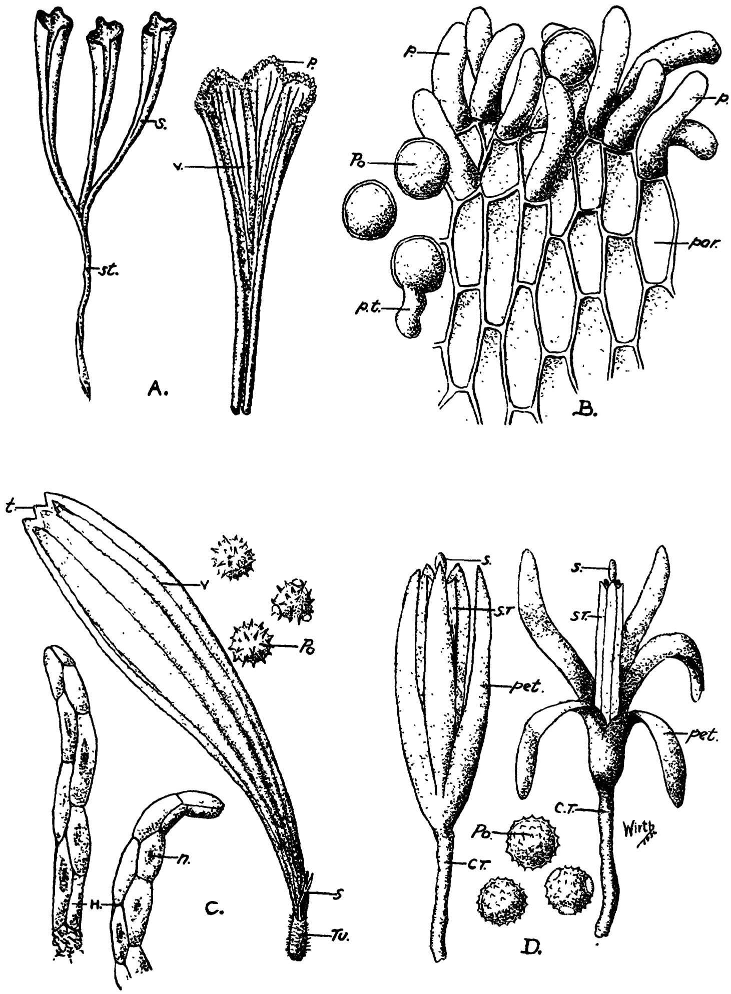


FIG. 70.—*A*, *Crocus sativus*, showing the three cornucopia-shaped stigmas (*s*) attached to the style (*st*), and the upper portion of the stigma enlarged to show venation (*v*) and papillæ (*p*). *B*, upper end of the stigma showing elongated parenchyma (*par*), cylindrical papillæ (*p*) up to 150 microns long and spherical pollen grains (*po*), 40 to 120 microns in diameter, and which occasionally exhibit a pollen tube (*pt*). *C*, ligulate floret of *Calendula officinalis*, 1- to 3-toothed (*t*) and 4- to 5-veined (*v*), showing a hairy tube (*Tu*) enclosing a bifid stigma (*s*). Microscopic identity characteristics are the non-glandular hairs (*H*) up to 950 microns in length and consisting of a double row of cells, often showing nuclei (*n*) and sharply spinose pollen grains (*Po*) up to 45 microns in diameter and often exhibiting three pores. *D*, disk floret of *Carthamus tinctorius* showing petals (*pet*) united below into a corolla tube (*CT*), the stamen tube (*ST*) and stigma (*s*). The pollen grains (*Po*) are somewhat spinose and vary between 50 and 100 microns in diameter. Both calendula and carthamus are adulterants of or substitutes for crocus. (Drawings by E. H. Wirth.)

3. Contains not more than 14 per cent of moisture.
4. Imparts a yellow color to water, alcohol, methanol, ether and chloroform, but not to xylene, benzene or carbon tetrachloride.
5. This color is removed by filtration through charcoal (*absence of coal tar dyes*).
6. When pressed between white filter paper, no translucent oily spots appear (*absence of fixed oil or glycerine*).
7. Ligulate or tubular florets and spinose pollen grains under microscopic examination are absent (*florets from the Compositæ*).
8. A 1 in 10,000 filtered macerate of crocus in water approximates that of hundredth-normal potassium dichromate, both in tint and strength of color (*exhausted saffron or artificial coloring*).
9. In sulfuric acid the stigmas immediately become blue, gradually change to purple, and finally to purplish-red. Composite florets do not assume such coloring.

The usual adulterants are indicated above.

Crocus has been used as a diaphoretic, an emmenagogue, and to promote eruption in measles, but its use for these purposes, other than as a domestic remedy, has been abandoned. Its employment today is principally as a coloring and flavoring agent.

Carthamus, American Saffron, Safflower or Indian Safflower (U. S. P. 1820 to 1882) is the tubular florets of *Carthamus tinctorius* (Fam. *Compositæ*). Its characteristics are shown in Figure 70, *D*. It is of a lighter red color than Crocus, but may be admixed with it and is frequently substituted for it. Carthamus is used medicinally for about the same purposes as crocus.

ORRIS

Orris, or Orris Root (U. S. P. 1820 to 1873; N. F. 1916 to date) is the peeled and dried rhizome of *Iris florentina* Linné, *Iris germanica* Linné, or *Iris pallida* Lamarck. Iris is from the Greek, meaning goddess of the rainbow, and alludes to the varied colors of the flowers; *florentina* relates to the city of Florence; *germanica*, of Germanic origin; and *pallida* from the Latin *pallidus*, pale, referring also to the color of the flowers.

The plant consists of a horizontal branching, thick, annulated rhizome bearing numerous broad sword-shaped leaves and long-peduncled flowers. In *Iris germanica* the sepals are dark violet-purple with a yellow beard and three lilac-colored petals about the same size as the sepals. The flowers of *Iris pallida* are pale blue-white; *Iris florentina* produces large white flowers and has the most fragrant root. *Iris germanica* and its varieties are cultivated almost universally as garden plants. Production of orris root takes place largely in Italy, although some is produced in France, Germany and in northern Africa. The rhizomes are dug in the early fall, those from three-year-old plants being preferred. The leaves and roots are removed and the rhizomes peeled and allowed to dry slowly in the sun, during which the fragrant odor is developed. There are two principal varieties, Florentine and Verona, the former being preferred. Orris root was employed in perfumery in Greek and Roman times. During the Middle Ages, Florence was an important source of the drug, the coat of arms of that city bearing a white iris against a red shield.

Description, Structure and Powder.—See Figure 71 and the National Formulary.

Constituents.—Orris "butter," a yellowish concrete volatile oil, 0.1 to 0.2 per cent, consisting mostly of myristic acid, and which owes its very fragrant odor to the ketone, irone; iridin, a crystalline glucoside, soluble in hot alcohol; an acrid resin and some tannin.

Standards.—Not more than 1 per cent of foreign organic matter, nor more than 1 per cent of acid-insoluble ash. Powdered orris is free from foreign starch, stone cells, sclerenchyma fibers and tannin masses; corky epidermal tissue indicates insufficient peeling. Effervescence with hydrochloric acid indicates liming.

Uses.—Powdered Orris Root is used in dusting powders, sachet powders, dentifrices, and toilet powders. The volatile oil is used in perfumery, both as a fixative and in violet combinations.

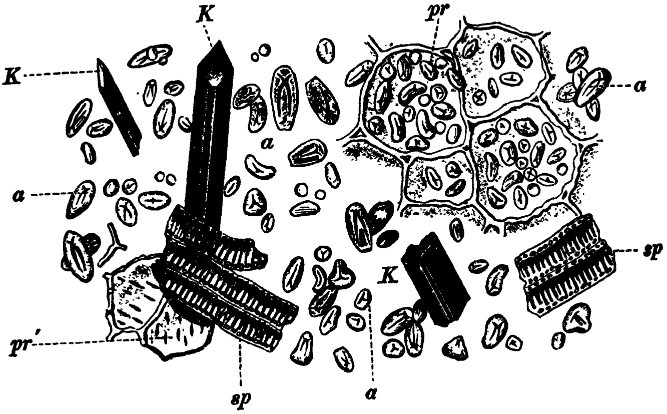


Fig. 71.—Powdered Orris Root. Light yellow with numerous fragments of starch-bearing parenchyma (*pr*); starch grains (*a*) ovoid, oval, truncate, some curved or with irregular protuberances, mostly single, from 10 to 50 microns in length, and with X- or scissors-shaped cleft in the large rounded end of the grain, two of the fissures extending into the small end of the grain; tracheæ (*sp*) showing spiral, annular, reticulate or scalariform markings, and up to 25 microns in width; parenchyma (*pr'*) with narrow oblique pores; calcium oxalate in prisms (*K*) up to 500 microns in length and 30 microns in width. (After Vogl.)

Blue Flag (U. S. P. 1820 to 1895; N. F. 1916 to 1942) is the dried rhizome of *Iris versicolor* Linné, or of *Iris virginica* Linné. The plant is herbaceous, growing in low swampy places in eastern and central North America. The rhizomes are freed from the scaly decayed leaves and roots, frequently sliced lengthwise, and dried.

The rhizome is cylindrical, more or less flattened, occasionally branched; outer surface annulate with numerous stem-scars on the upper surface and numerous root-scars on the lateral and under portions; externally grayish brown to blackish brown and occasionally with the fibrous bases of decayed leaves and short fragments of the stout roots; fracture short, resinous; internally reddish brown, with a distinct yellowish endodermis and numerous, whitish, scattered vascular bundles (see Fig. 72). The powdered drug is pale reddish brown, odor slightly aromatic; taste sweetish, bitter and slightly acrid; calcium oxalate in solitary prisms up to 350 microns long; tracheæ with spiral or reticulate markings; parenchyma with numerous resin cells; amylodextrin grains small, colored reddish with iodine; true starch grains rare.

Blue Flag contains about 25 per cent of acrid resins and a small quantity of volatile oil. Total ash, about 3.5 per cent. "Irisin" or "iridin" is a mixture of the resins from the drug.

Blue Flag contains not more than 5 per cent of attached roots and leaf-bases and not more than 2 per cent of other foreign organic matter, and yields not more than 2 per cent of acid-insoluble ash. The drug on the market varies considerably owing to the lack of uniformity in its collection. The constituents are apparently very labile, the resins becoming changed to insoluble and inert substances.

Blue Flag is a cathartic, also an emetic and a diuretic. Average dose, 2 gm.

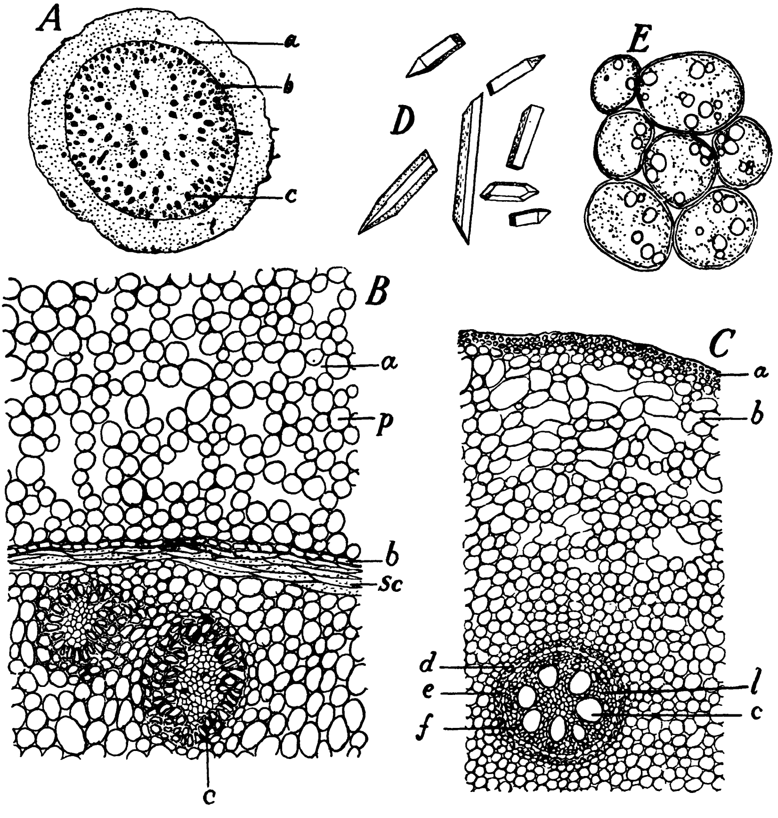


FIG. 72.—Rhizome of *Iris versicolor*. *A*, diagram of transverse section showing vascular bundles (*a* and *c*); endodermis (*b*). *B*, portion of rhizome showing parenchyma (*p*); intercellular spaces (*a*); endodermis (*b*), closed ring of tangentially elongated sclerenchymatous fibers (*Sc*); concentric vascular bundle of the leptocentric type (*c*). *C*, transverse section of root showing epidermis (*a*); cortical parenchyma (*b*); central stele with endodermis (*d*); pericambial layer (*e*); phloem (*l*); tracheæ (*c* and *f*), those at the periphery being smaller. *D*, crystals of calcium oxalate. *E*, cells of parenchyma with amylodextrin starch grains, *i. e.*, becoming reddish with solution of iodin. (After Bastin.)

ZINGIBERACEÆ, OR GINGER FAMILY

This family consists of about 300 species of perennial herbs characterized by long or tuberous rhizomes and strongly thickened roots. They are indigenous to the tropics of the eastern hemisphere, especially the countries bordering the Indian Ocean and Malay Islands, only two of the genera being found in tropical America. The leaves are lanceolate and ligulate at the basal portion of the petiole. The walls of the cells of the endodermis are thin and mostly suberized. The plants usually contain a volatile oil colored yellow by curcumin, and found in special secretion cells which resemble the surrounding parenchyma. The starch grains are quite characteristic, having a distinct acute termination or beak near the hilum.

GINGER

Ginger (U. S. P. 1820 to date) is the dried rhizome of *Zingiber officinale* Roscoe known in commerce as Jamaica Ginger and African Ginger. *Zingiber* is from the Arabic *Zindschebil,* meaning root of *Zindschi* (India). The specific name refers to its being for sale in the shops.

While the U. S. Pharmacopœia did not distinguish the several commercial kinds of ginger in the revisions from 1820 to 1882, yet a quotation from the U. S. Dispensatory of 1833 indicates that several commercial varieties were in use: "The *common, East India* or *black ginger* is dark ash color or almost black. It is most extensively used in the United States. The *Jamaica* or *white ginger* is entirely deprived of its epidermis and is white or yellowish-white on the outside. It produces a beautiful yellowish-white powder and has more of the sensible qualities of ginger than the black variety."

In the Pharmacopœias of 1882, 1894 and 1905 the definition required that the rhizome be "deprived of the corky layer," indicating Jamaica ginger.

In the U. S. P. of 1916, Jamaica, limed Jamaica, African, Cochin, Calcutta, Calicut, and Japanese gingers were recognized by name.

In the U. S. P. of 1926, Jamaica, African and Cochin gingers were recognized.

African Ginger is not so completely peeled as is Jamaica ginger; it may be scraped on its two lateral surfaces, is darker in color, both externally and internally, more pungent in taste and with a less delicate flavor than the Jamaica ginger.

Cochin Ginger somewhat resembles African ginger, but is usually larger, well scraped, contains more starch and breaks with a shorter fracture.

Calcutta and **Calicut Ginger** (possibly the same) resemble African, but are somewhat larger and more corky.

Japanese Ginger is obtained from *Zingiber mioga.* The rhizome is usually limed and is considerably smaller and less pungent than Jamaica ginger; it has a somewhat bergamot-like odor.

Martinique Ginger, never U. S. P., is said to be derived from *Zingiber zerumbet.*

Preserved Ginger is the peeled, fresh rhizomes preserved by boiling in syrup. The West Indian product is used as a delicate spice. That from China may be prepared from Galangal.

The ginger plant (see Fig. 73) is propagated in Jamaica by rhizome cuttings which are planted in March and April. The rhizomes are dug and peeled in December and January. As quickly as peeled, the rhizomes are washed in water for hours, then dried in the sun for five or six days, being covered at night or during rainy weather.

Ginger was known in China as early as the fourth century B.C. It was used as a spice by the Greeks and Romans, who considered it an Arabian product because it came to them among spices from India by the way of the Red Sea. From the eleventh to the thirteenth century it was a common import from the East. Marco Polo observed it in China and India, 1280–90. Ginger was introduced into Jamaica and other

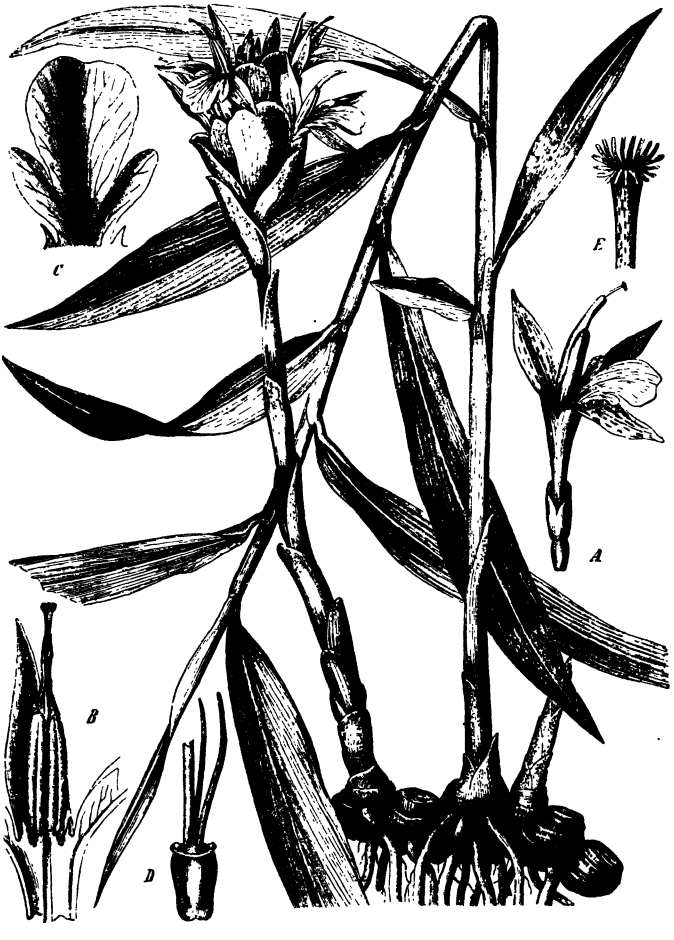


FIG. 73.—*Zingiber officinale*, the rhizome of which constitutes the Ginger of the market. Entire plant showing rhizome and roots, a leaf-branch and a flower-branch, also scars of previous year's growth after decay of leaf- and flower branches. *A*, entire flower; *B*, section of flower showing beak-like appendages at the summit of the fertile stamen, which encloses the style; *C*, 3-parted labellum or irregular segment of corolla showing two tooth-like staminodes (rudiments of stamens) at the base; *D*, the ovary with lower portion of style and two epigynous filiform processes which secrete nectar; *E*, summit of funnel-shaped, fringed stigma. (After Berg and Schmidt.)

islands of the West Indies by the Spaniards, and exports from the West Indies to Spain appear in considerable quantity as early as 1547.

DESCRIPTION, STRUCTURE AND POWDER.—See Figure 74, and the U. S. Pharmacopœia.

CONSTITUENTS.—Ginger contains a volatile oil (1 to 3 per cent) to which its aroma is due; a viscid oily resinous liquid known as "gingerol" (0.5 to 1.5 per cent) to which its pungency is due; resins, starch and mucilage. Gingerol consists of several homologous phenols which are destroyed by boiling with dilute alkalis.

STANDARDS.—Ginger contains not less than 42 per cent of starch, not more than 8 per cent of crude fiber, not more than 1 per cent of lime (CaO), not less than 12 per cent of cold water extractive, not less than 4.5 per cent of ether-soluble extractive, not less than 2 per cent of non-volatile ether extractive, not more than 7 per cent of total ash, not more than 2 per cent of ash insoluble in hydrochloric acid, and not less than 2 per cent of ash soluble in cold water. Limed ginger (bleached ginger) contains not more than 4 per cent of CaO and not more than 10 per cent of total ash, and conforms in other respects to the above standards.

USES AND DOSE.—Ginger is a condiment, an aromatic stimulant and a carminative. Average dose, 0.6 gm.

ADULTERANTS.—Since the strict enforcement of the National Pure Food and Drug law, adulterated ginger seldom appears in American commerce. Previous to the enforcement of this law, ginger, especially when powdered, was subject to extensive adulteration. Among the adulterants were starches, cereal products, sawdust, curcuma to restore color, capsicum to increase pungency, exhausted ginger, and excessive liming. Unpeeled gingers contain numerous corky fragments.

The most dangerous adulterants ever known in commerce were tricresyl phosphate and triethylene glycol added to a "cheap" fluid ginger of high alcoholic concentration and sold to alcohol addicts during the prohibition era in the United States. Before enforcement officials had discovered and stopped this adulteration perhaps 16,000 persons suffered from paralysis or death from drinking this concoction.

Galangal or Galanga (N. F. 1916 to 1936) is the rhizome of *Alpinia officinarum*, a plant indigenous to the countries of eastern and southeastern Asia and cultivated there since ancient times. The generic name *Alpinia* was given in honor of an Italian botanist. The sympodially branching rhizome may attain a length of one meter and is collected from plants that are from four to ten years old. It is cut into small pieces and dried. The commercial supplies are obtained from Hainan and shipped from Shanghai and Hangchow, China.

The rhizome is nearly cylindrical, distinctly branched, in pieces from 2 to 10 cm. in length and from 7 to 20 mm. in diameter; externally it is reddish brown; the odor is aromatic, and the taste is aromatic and pungent.

The powder is reddish brown and displays numerous ellipsoidal, ovoid, more or less spatulate starch grains from 10 to 60 microns in length, having a circular hilum at the broad end and indistinct lamellæ; numerous yellowish red secretion cells frequently separated from the starch-bearing parenchyma; non-suberized secretion cells with a dark brown, amorphous, tannin-like content; parenchyma with porous walls and occasionally without starch; fragments of tracheæ with unlignified porous walls or scalariform or reticulate thickenings; adjoining sclerenchymatous fibers non-lignified; no cork cells.

Galangal contains from 0.5 to 1 per cent of a cineol-containing volatile oil; a soft acrid resin containing a pungent principle, galangol; three yellowish crystalline principles, alpinin, galangin, and cæmpferid, each occurring to the extent of about 0.1 per cent; starch from 20 to 25 per cent; and ash, containing manganese, 4 per cent.

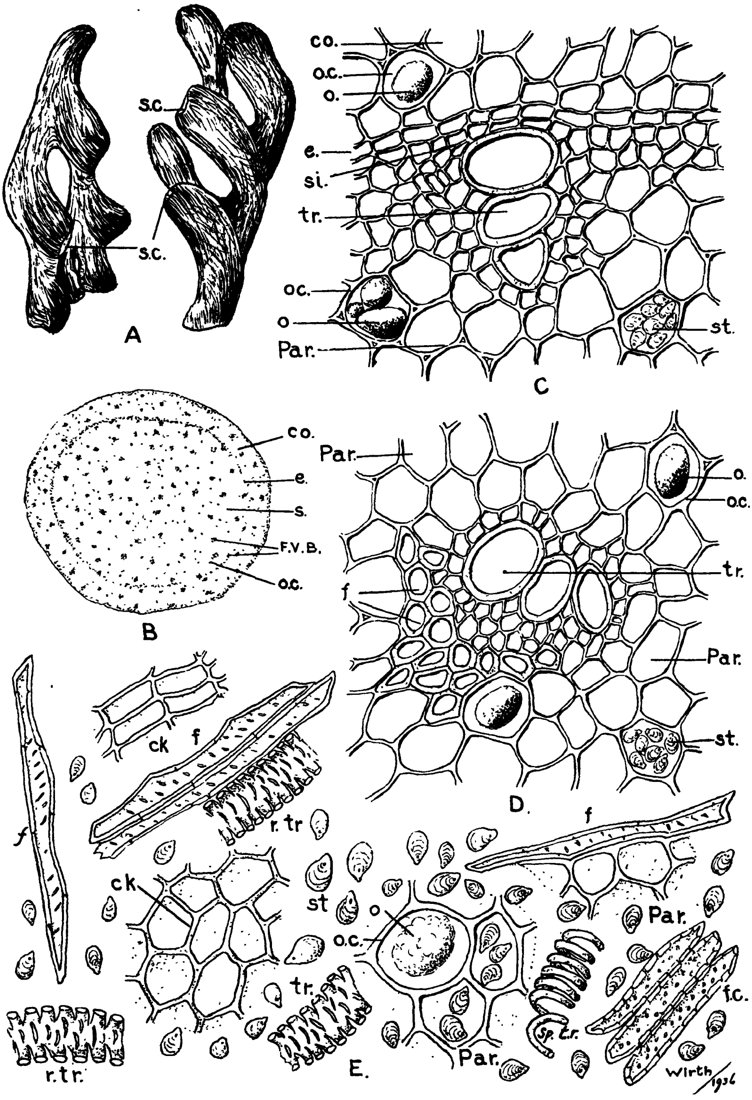


FIG. 74.—Jamaica Ginger. *A*, irregularly branched rhizomes (4 to 16 cm. long and 4 to 20 mm. in thickness) from which the cork has been removed, showing depressed stem scars (*sc*) at the ends of the branches; the rhizomes are longitudinally striate, somewhat yellowish to light brown in color, break with a short-fibrous, starchy-resinous fracture. and have an aromatic odor and a pungent aromatic taste. *B*, lens view of a transverse section; *C*, transverse section through a bundle and the surrounding region near the endodermis; *D*, transverse section through one of the inner bundles: *Co*, cortex; *e*, endodermis; *s*, central cylinder; *FVB*, fibrovascular bundle; *oc*, oil cells; *par*, parenchyma; *tr*, tracheæ; *f*, fibers; *si*, sieve; *o*, oleoresin; *st*, starch. *E*, elements of the powder; the starch (*st*) is from 5 to 60 microns in diameter and the fibers are very undulate in character, have oblique pores and are unlignified; tracheæ (*tr*), are scalariform, reticulate (*r*) or spiral (*sp*) and are frequently unlignified; fiber-like cells (*fc*) with suberized walls are occasionally present; cork cells (*ck*) should be absent. (Drawings by Wirth.)

Galangal is an aromatic stimulant, a condiment and a carminative. Average dose 1 gm.

Zedoaria or Zedoary (N. F. 1916 to 1936) is the dried rhizome of *Curcuma zedoaria*, a plant cultivated in southeastern Asia, Madagascar and other tropical countries. It is exported mostly from Ceylon and Madras.

The rhizome, before drying, is cut transversely into nearly circular disks. When dried these are 1 to 4 cm. in diameter and 4 to 10 mm. in thickness, nearly white on the cut surfaces and yellowish brown on the edge; fracture short and mealy; odor aromatic and camphoraceous; taste pungent and somewhat bitter.

The powdered drug shows non-glandular, multi-celled epidermal hairs, up to 1 mm. long, and possessing very thick walls; starch grains abundant, 10 to 75 microns long and resembling ginger starch; suberized oil cells with a colorless content, rather than the yellow oil cells of ginger.

Zedoary contains from 1 to 1.8 per cent of a cineol-containing volatile oil; a soft resin; 50 per cent of starch; 4.5 to 7.5 per cent of ash and small quantities of sugar, fixed oil and mucilage.

Zedoary is an aromatic stimulant and a carminative. Average dose, 1 gm.

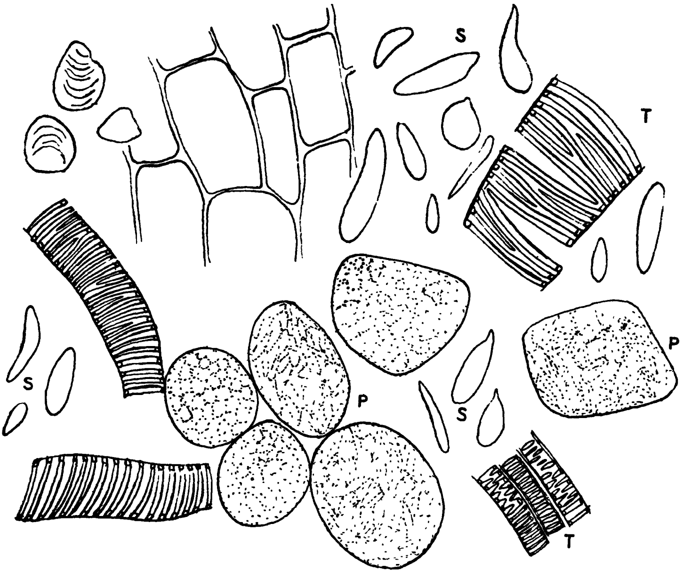


FIG. 75.—Curcuma (Turmeric): *P*, fragments of parenchyma containing curcumin and swollen and altered starch grains which form an indistinguishable mass within the cells and constitute the greater proportion of the powder; *T*, tracheæ; *S*, unaltered starch grains.

Curcuma or Turmeric (U. S. P. 1820 to 1882) is the prepared rhizome of *Curcuma longa* Linné. The plant is cultivated in many tropical countries, principally China, India, and Java, by methods similar to those used in the cultivation of ginger. The rhizomes are collected at the end of the growing season, cleaned, boiled for some hours, and then carefully, but rapidly, dried in the open air.

"Round Curcuma," from the swollen internodes, is ovoid and up to 2 cm. thick; "Long Curcuma," from the fleshy rhizome branches, is cylindrical or fusiform and up to 5 cm. long. The drug is orange yellow in color, somewhat darker externally; odor aromatic; taste pungent and somewhat bitter.

The parenchyma cells of cortex and pith contain curcumin and starch paste, in which long, lens-shaped, unaltered starch grains are occasionally present. The oil cells have suberized walls and contain colored volatile oil globules and resin masses.

The powder is bright yellow; see Figure 75.

Curcuma contains from 1 to 5 per cent of an orange-yellow, somewhat fluorescent volatile oil; about 0.3 per cent of curcumin, which crystalizes in orange-red, short rods or prisms having a beautiful blue refraction, and is freely soluble in alcohol, ether, fixed and volatile oils, imparting a bright yellow color to them; from 30 to 40 per cent of starch; 4 to 7 per cent of ash; and a small quantity of a fixed oil.

Curcuma is used as a coloring agent and a condiment and is also an aromatic stimulant and carminative. Average dose, 0.5 gm.

Powdered turmeric is extensively used as a coloring agent for mixtures of powders and for certain food preparations, particularly "Prepared Mustard." Its principal microscopic identity feature consists of the starch cells containing curcumin and which are bright yellow in color, but become reddish brown upon treatment with alkali, crimson with strong, sulfuric acid, and blue with iodine.

As alternative tests for the detection of curcuma the following are useful:

1. Place a few drops of a mixture of equal parts of concentrated sulfuric acid and 95 per cent alcohol on a slide which lies against a white background. Sprinkle a small quantity of the suspected powder into the reagent; view it with the hand lens: the particles of turmeric will turn red, the color gradually flowing out into the surrounding liquid.

2. Stir a small quantity of the suspected powder into a thin paste with a mixture of ether and chloroform. Allow this paste to dry on filter paper and when dry remove the powder and treat the remaining yellow stain with hot saturated boric acid solution. An orange-red color is produced which turns bluish black upon the addition of ammonia, if curcurma is present.

CARDAMOM

Cardamomum (U. S. P. 1820 to 1916) and **Cardamomi Semen, or Cardamom Seed** (U. S. P. 1916 to date) is the dried ripe seed of *Elettaria Cardamomum* Maton, recently removed from the capsules.

Cardamom fruit was recognized on the basis that the seed deteriorated less rapidly when preserved within the capsule; it is the seed that has been used, after recent removal from the capsules, throughout the whole period of Pharmacopœial recognition.

Eletteria is the native name of the plant in Malabar; *cardamomum* is the ancient classical name for the spice.

The plant is a reed-like perennial herb rising 2 to 3 meters high from a thick horizontal rhizome, bearing long lanceolate leaves and short scapes with racemes of greenish white flowers. It is cultivated in Indo-China, Ceylon and along the Malabar coast. The fruits are collected mostly from October to December as they ripen. They are sun-dried, bleached with sulfur dioxide and graded, those with a split capsule furnishing separated seed for the distillation of the oil.

Cardamoms were mentioned in the early Sanskrit writings of Susruta and appear in the list of dutiable Indian spices in Alexandria in A.D. 176 to 180. The Portuguese navigator Barbosa (1514) first definitely described them as a product of the Malabar coast. The date of their introduction into Europe is difficult to determine as many of the cardamoms mentioned in early writings may have been Amomums.

Cardamom Fruit are ovoid capsules, 1 to 2 cm. in length, loculicidally dehiscent and of a light tan color. Unbleached fruit are darker and blotched.

The fruit are graded according to size and shape into "longs, short-longs, mediums, shorts and tiny." Commercially they are classed according to the district where they originated: (1) Mysore, principally obtained now from Mysore-type of plants grown in Ceylon; (2) Malabar, obtained largely now from Malabar-type plants cultivated in Ceylon; (3) Mangalore, on the Malabar coast; and (4) Alleppy, grown in Travancore and Cochin. The Ceylon fruit grade the highest in quality.

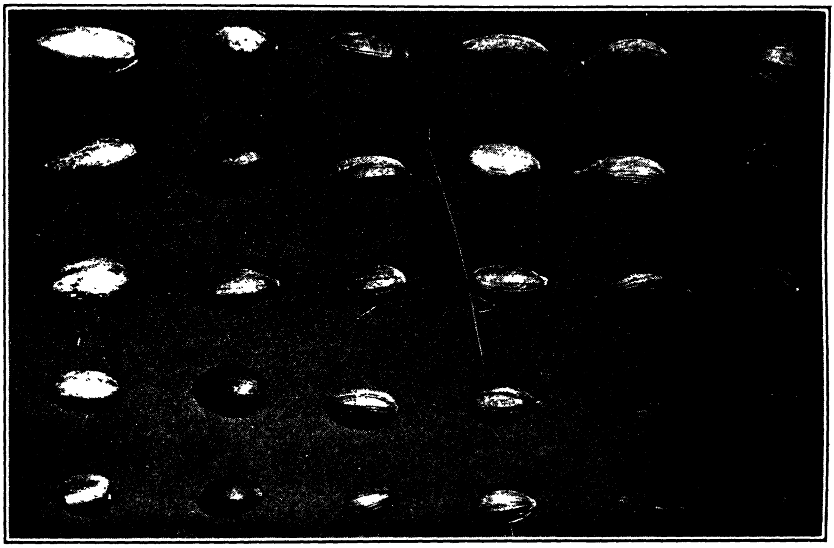


FIG. 76.—Commercial Cardamoms. *A*, Mysore; *B*, Malabar; *C*, Mangalore; *D*, Madras; *E* Allepy; *F*, Siam. *1*, "longs"; *2*, "short-longs"; *3*, "mediums"; *4*, "shorts"; *5*, "tiny."

DESCRIPTION, HISTOLOGY AND POWDER.—See Figures 76, 77, and the U. S. Pharmacopœia.

CONSTITUENTS.—Of the Seed: volatile oil, 3 to 6 per cent; fixed oil, about 10 per cent; starch; calcium oxalate; and total ash 4 to 8 per cent. It yields not more than 5 per cent of acid-insoluble ash.

USES.—Cardamom seed is an aromatic stimulant, a carminative, a condiment and a flavoring agent. Oil of cardamom is used chiefly as a flavoring agent; pharmaceutically, in certain official spirits.

Cardamom Oil (N. F. 1916 to date) is a volatile oil distilled from cardamom seed.

DESCRIPTION, TESTS AND STANDARDS.—See the National Formulary.

ADULTERANTS.—**Cardamom husk,** the pericarp of the fruit, has been used as an adulterant of not only powdered cardamom seed but also of other powdered drugs. It may be identified microscopically by lignified fibers having relatively thin walls and slightly oblique pores; spiral tracheæ and an abundance of parenchyma cells, some of which contain calcium oxalate. **Powdered Ginger** may be distinguished by the characteristic starch and non-lignified fibers. Powdered cardamom is subject to the usual adulterants of spices.

ALLIED PLANTS.—**Ceylon Cardamom** is obtained from wild plants of *Elettaria cardamomum* var. *major*. The capsules are 2 to 4 cm. long and about 10 mm. in diameter, distinctly triangular in transverse section, deeply longitudinally striate and slightly pubescent. In each loculus there are about 20 seeds, which are about 4 mm. long, bitter and less aromatic than the official cardamom.

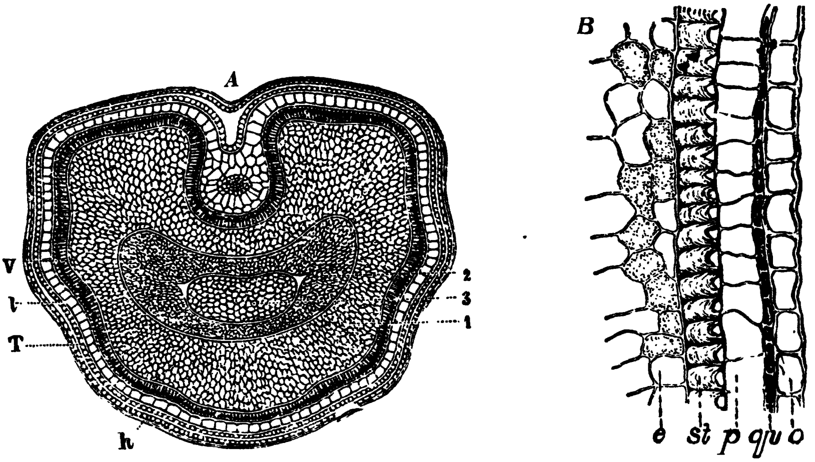


FIG. 77.—Cardamom Seed: *A*, transverse section showing the arillus (*h*), the several layers of the seed coat (*T*, *l*, *V*), perisperm (*1*), endosperm (*2*) and embryo (*3*) at the center. *B*, transverse section of the seed coat and perisperm of Malabar cardamom showing epidermal cells (*o*), cells having a brown content (*qu*), cells containing ethereal oil (*p*), brown stone cells (*St*) with very thick inner walls, and perisperm (*e*). (*A*, after Meyer; *B*, after Moeller.)

Siam Cardamom (see Fig. 76) is obtained from *Amomum cardamomum* growing in Siam and Java, and known as cluster cardamoms; *Amomum xanthoides* yields the **bastard** or **wild Siamese Cardamom**; *Amomum aromaticum* yields the **Bengal** and **Nepal Cardamoms** and *Amomum maximum* the **Javanese Cardamom.**

Grains of Paradise are the seeds of *Aframomum melegueta,* widely distributed in tropical Africa. The seeds are somewhat pyramidal in shape, exhibit a pitted testa and possess a very pungent taste. The pungency of the seeds is due to paradol, a substance very closely related to gingerol. Other African species of *Aframomum* yield cardamom-like fruits among which the following might be mentioned: **Abyssinian Cardamom** from *A. korarima;* **East African Cardamom** from *A. mala;* **Cameroon Cardamom** from *A. hanburii;* and **Madagascar Cardamom** from *A. angustifolium.*

MARANTACEÆ, OR ARROWROOT FAMILY

Plants of this family are mostly perennial herbs having thick fleshy rhizomes or tubers. They are found mostly in the tropics and are represented by about 150 species. The leaves are long-petioled and characterized by a swollen, long, sac-like sheath at the base. Sections of the leaf show a hypodermis with unusually large cells. The petiole of the stem contains large lysigenous lacunæ, and star-shaped parenchyma is developed in the diaphragms. Calcium oxalate occurs in the form of rod-like crystals.

Maranta, Arrowroot Starch, Bermuda Arrowroot, or St. Vincent Arrowroot (U. S. P. 1820 to 1882; as reagent, U. S. P. and N. F. 1936 to date) is the starch obtained from the rhizome of *Maranta arundinacea,* a plant indigenous to the West Indies and northern part of South America, and now extensively cultivated in nearly all tropical countries.

One-year-old rhizomes are collected, washed, beaten into a pulp, mixed with water, and the starch removed by filtering through copper sieves; this is then carefully dried. The commercial supplies come chiefly from St. Vincent and Bermuda. The yield is about 20 per cent of dried starch from the fresh rhizomes.

Bermuda arrowroot is in hard, irregular granules or masses, from 1 to 6 mm. in diameter; it is easily reduced to a smooth powder, which is velvety to the touch. The starch grains (Fig. 46) are ellipsoidal to ovoid or oblong, 10 to 65 microns in length, the lamellæ mostly indistinct, and the transverse or crescent-shaped cleft at the middle or near the broad end of the grain.

St. Vincent arrowroot is slightly darker in color, and the masses are sometimes 20 mm. in diameter. The grains having clefts are more numerous. The arrowroot starches show a distinct cross with the micropolariscope and a marked play of colors when a selenite plate is used.

Maranta contains about 10 per cent of water and less than 1 per cent of ash. It enters largely into infant and convalescent foods and should be as free as possible from impurities. Upon boiling 1 part of starch with 10 parts of diluted hydrochloric acid for ten minutes, with occasional shaking of the mixture and filtering, the starch grains should not become agglutinated nor the filtrate mucilaginous, nor should an unpleasant odor be emitted. When examined on the thermo-stage of the microscope the granules begin to swell at 70° C. One part of starch heated to 100° C. with 20 parts of distilled water gives a transparent, mucilaginous mixture which is practically free from odor.

So-called **American Arrowroot** consists of one of the other commercial starches, as potato or corn, and may be readily detected by means of the microscope (Fig. 46).

The name arrowroot is applied to the starches obtained from a number of different plants. **Tahiti Arrowroot** is obtained from *Tacca pinnatifida;* **East Indian Arrowroot** is prepared from several species of *Curcuma;* **South Sea Island Arrowroot** is obtained from several species of *Arum* and *Dioscorea;* **Brazilian Arrowroot** is identical with cassava or tapioca starch.

ORCHIDACEÆ, OR ORCHID FAMILY

On account of the remarkable beauty and delicacy of the flowers, this family, comprising about 12,000 species, is probably the most interesting group in the entire plant kingdom. The species are widely distributed, although most abundant in the tropics. They are sometimes classified according to habit of growth, as saprophytic, epiphytic and terrestrial. Most of the orchids common to the United States are either saprophytic or terrestrial plants. The epiphytic orchids are characteristic of the tropics and are by far the most valuable of the orchids. They are sometimes spoken of as parasitic, but this is erroneous, as none of the members of this family is parasitic. The stems show a characteristic monocotyledonous structure. Mucilage, in the form of a cell-content, occurs in those genera producing tubers. Similar mucilage cells are also found in the leaves, and also in the roots of the epiphytic forms.

VANILLA

Vanilla or Vanilla Bean (U. S. P. 1863 to 1916; N. F. 1916 to date) is the cured, full-grown, unripe fruit of *Vanilla planifolia* Andrews, known in commerce as Mexican or Bourbon Vanilla, or of *Vanilla tahitensis* Moore, known in commerce as Tahiti Vanilla. *Vanilla* is from the Spanish *vania*, a sheath-like pod, and *illa*, small; *planifolia* from the Latin *planus*, flat, and *folium*, leaf; *tahitensis*, in reference to Tahiti, its adopted home.

The plants are perennial, climbing, dioecious epiphytes attaching to the trunks of trees by means of aerial rootlets. The plant is native to the woods of eastern Mexico but is cultivated in tropical countries where the temperature does not fall below 18° C. and where the humidity is very great.

The plant is usually propagated by means of cuttings and after two or three years reaches the flowering stage, continuing to bear fruit for thirty or forty years. The flowers are hand-pollinated, about 30 flowers on each plant, thus producing larger and better fruits. The fruits are collected as they ripen to a yellow color, six to ten months after pollination and are cured by dipping them in warm water and repeatedly sweating them between woolen blankets in the sun during the day and packing them in wool-covered boxes at night. This requires about two months, during which the pods lose from 70 to 80 per cent of their original weight and take on the characteristic color and odor of the commercial drug. The pods are then graded, tied into bundles of about 50 to 75, and these are sealed in tin containers for shipment.

The Spaniards found vanilla in use as a flavor for cocoa among the Aztecs of Mexico and introduced its use into Europe. Cultivation was begun in Reunion in 1839, and followed shortly after in other countries.

Description and Structure.—See Figure 78 and the National Formulary. Tahiti Vanilla, grown in Tahiti and Hawaii, is reddish brown in color, about as long as the Mexican but sharply attenuated and twisted in the lower portion. The odor is somewhat unpleasant and the variety is somewhat unsuitable for flavoring.

Constituents.—Green vanilla contains two glycosides, glucovanillin (avenein) and glucovanillic alcohol, the former being hydrolyzed by an enzyme during the curing process, into glucose and vanillin; the latter being similarly hydrolyzed into glucose and vanillic alcohol which is in turn oxidized to vanillic aldehyde (vanillin). Vanillin is the principal flavoring constituent. Vanilla also contains about 10 per cent of sugar; 10 per cent of fixed oil and calcium oxalate.

Standards.—Vanilla yields not less than 12 per cent of anhydrous extractive soluble in diluted alcohol.

Upon heating vanilla, a microsublimate of vanillin forms in droplets which crystallize into tufts upon rubbing, and may be readily identified by microchemical tests (page 188).

Place a few of the crystals occurring as an efflorescence on the fruit of a microscopic slide or watch crystal; add a drop of phloroglucinol T.S. and a drop of hydrochloric acid: the solution immediately acquires a carmine-red color (*distinction from benzoic acid*). Exhausted and redried vanilla pods or pods of poor quality are sometimes dusted with crystals of benzoic acid to simulate a drug of good quality. Benzoic acid as well as coumarin may be detected by their micromelting points (see Fig. 80).

Uses.—Vanilla is extensively used as a flavoring agent. It has been replaced to some extent, but by no means completely by synthetic vanillin. The latter does not completely represent the flavor or odor of the pods.

Commercial Varieties:

Mexican or Vera Cruz Vanilla is the best grade on the market, the pods frequently attaining a length of 30 to 35 cm. The supply is largely consumed in Mexico and the United States.

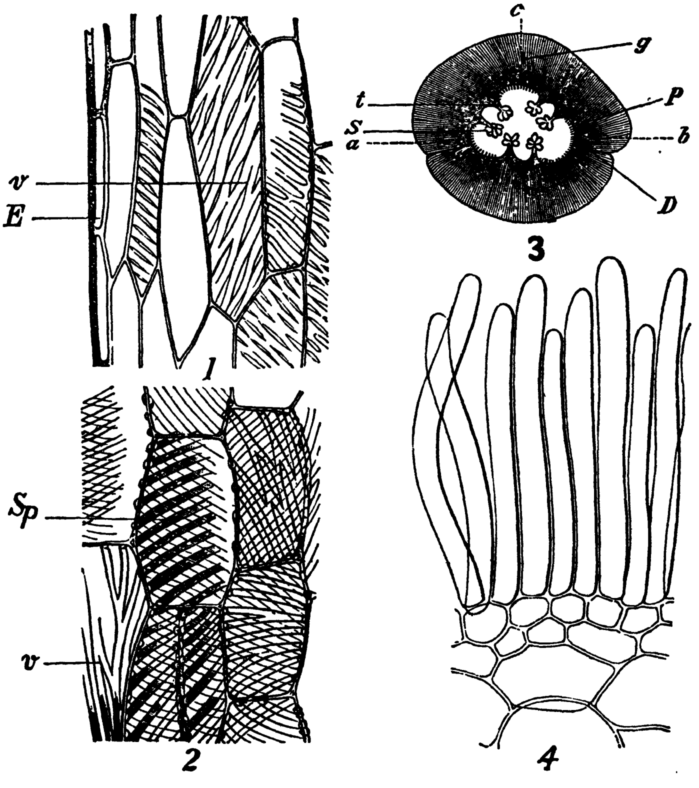


Fig. 78.—Vanilla: *3*, transverse section of an unripe fruit showing the three carpels (*a*, *b*, *c*), line of dehiscence (*D*), placenta (*t*), seeds (*S*), fibrovascular bundle (*g*), papillæ (*P*). *1*, radial longitudinal section of the outer part of the pericarp showing epidermis (*E*), and parenchyma cells with oblique pores (*v*). *2*, tangential longitudinal section of the outer part of the pericarp showing cells with oblique pores (*v*) and spirally thickened bands (*Sp*). *4*, inner layer of the pericarp showing the very long simple hairs or papillæ. (After Meyer.)

Bourbon Vanilla is produced in the Isle of Reunion. It resembles the Mexican variety, but is about two-thirds as long, blacker in color, usually covered with a sublimate of needle-shaped vanillin crystals and possess a tonka-like odor. Most of the supply goes to France, although some reaches the United States via that country.

Mauritius Vanilla, grown in the island of that name and in the Seychelles, occurs in cylindrical pods, somewhat lighter and shorter than Mexican. Most of the supply goes to London.

Venezuelan, Brazilian and other varieties of vanilla rarely reach this country.

Vanillons are the fruits of the wild vanilla plants and are used in the manufacture of tobacco and sachet powder. They are 10 to 12 cm. long, 1.5 to 2.5 cm. in diameter, gradually tapering toward each end, somewhat triangular in outline, externally dark brown to reddish brown, frequently with transverse markings, due to their being wrapped with twine during the process of curing, when they are spoken of as "braided," and generally longitudinally split; the odor is peculiar, somewhat resembling "heliotrope," and is due to the presence of the aldehyde, heliotropin (piperonal) which is closely related to vanillin.

Pompona Vanilla is the fruit of wild and cultivated plants of *Vanilla pompona*, which is considered to be the original plant from which *V. planifolia* has been derived by cultivation. The fruits resemble the vanillons in appearance, but the odor is disagreeable, like that of Tahiti vanilla.

Vanilla Splits and **cuts** represent the more mature fruits in which dehiscence has taken place and which are cut up into short lengths.

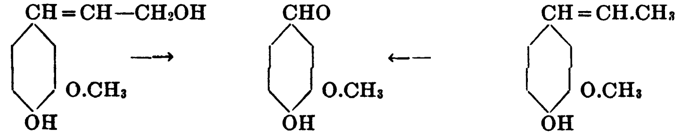
Allied Products.—The fruits of a number of other species of *Vanilla* yield vanillin, which is also found in the orchid, *Selenipedium chica*, of Panama; in the fruit of *Rosa canina* of northern and middle Europe; in the flowers of *Spiræa ulmaria;* in the balsams and resins of the genus *Toluifera* (see page 337); in the seeds of *Lupinus albus* of Europe and in the bulbs of *Dahlia.*

Tonka Bean (see page 342) has been used as an adulterant of powdered vanilla, or in combination with vanilla in its preparations. It contains the odorous principle coumarin which somewhat resembles vanillin.

A number of the orchids contain coumarin, and these belong chiefly to the genus *Orchis*, as *Orchis odoratissima* of Europe; *O. coriophora* of Europe and the Orient; *O. simia* of Europe and the Orient; *O. militaris* of Europe and Asia; *Habenaria conopsea* of Europe and Asia; *Aceras anthropophora* of Europe and Arabia.

Vanillin (U. S. P. 1905 to date; as a reagent, U. S. P. 1916 to 1926; N. F. 1926 to date) is methyl protocatechuic aldehyde and may be obtained from vanilla or prepared synthetically from other sources.

Preparation.—(1) In the preparation of vanillin from vanilla the pods are ground, mixed with sand and extracted with ether; the ethereal solution is then shaken with sodium sulfite solution from which the vanillin is liberated by treatment with sulfuric acid, expelling the sulfurous acid, extraction with ether and crystallization. (2) Coniferin, a glucoside present in the cambium sap of pines is treated with a dilute solution of potassium dichromate and sulfuric acid. This not only hydrolyzes the coniferin into glucose and coniferyl (vanillic) alcohol, but oxidizes the alcohol to the aldehyde, vanillin, which is purified by extraction with ether and subsequent crystallization. (3) Eugenol is acetylized to form acetyl-isoeugenol, which in turn is oxidized to acetyl-vanillin with potassium dichromate. The acetyl-vanillin is then hydrolyzed with alkali, acidified and removed from solution by shaking with ether. Most of the vanillin in commerce is made from eugenol, probably for economic reasons.



Coniferyl alcolol Vanillin Isoeugenol

Description.—Fine, white to yellow crystals having an odor and taste resembling vanilla. It is slightly soluble in water and glycerin and freely soluble in alcohol, chloroform and ether. It melts at 80° to 82° C.

Microchemistry.—1. Vanillin may be readily microsublimed or may be obtained from its solutions by crystallization on a slide (see Fig. 79).

2. When a drop of water and a drop of ferric chloride solution are added to a crystal of vanillin on a slide, covered with a cover-glass and carefully warmed, the crystal will first surround itself with a blue color and finally needles of dehydro-divanillin will form.

3. Hydrochloric or sulfuric acid with phenols (phloroglucin, orcin or resorcin) give a red coloration when applied to a crystal of vanillin on a slide. Since, however, many other substances give this reaction care must be employed in interpreting results.

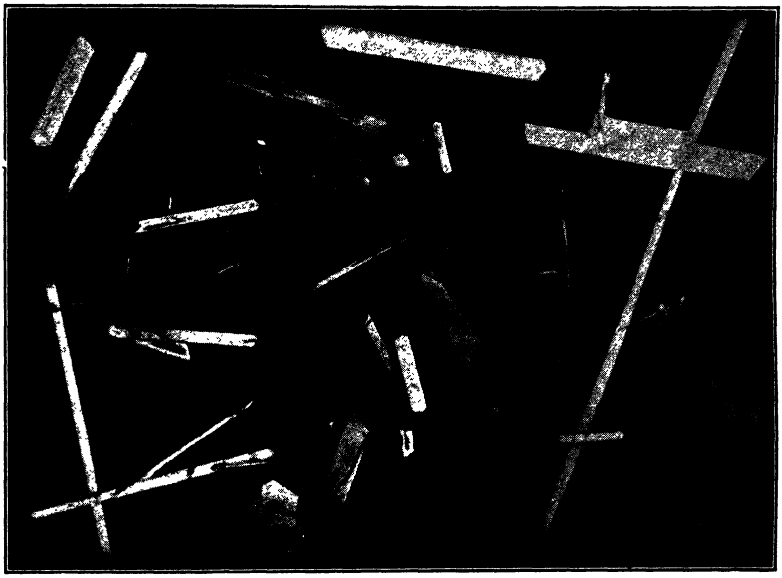


FIG. 79.—Vanillin, orthorhombic crystals obtained from saturated aqueous solution

4. The sublimate or crystallate of vanillin also gives the following reactions: (*a*) Potassium hydroxide gives bunches of needles; (*b*) *m*-phenylindiamin and hydrochloric acid gives orange needles; and (*c*) vanadic acid in phosphoric acid 1 to 4, gives orange to red-brown needles.

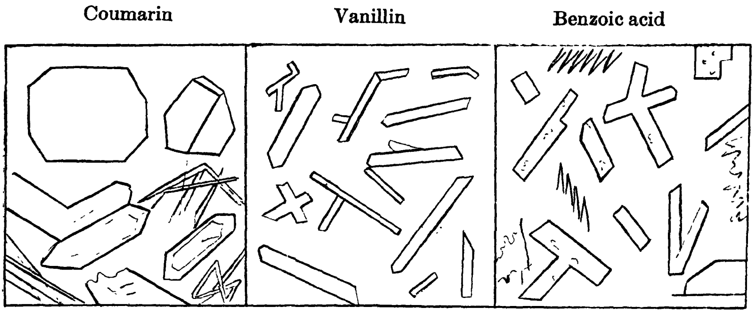
ADULTERANTS AND SUBSTITUTES.—1. Coumarin (see page 342), the principal constituent of tonka bean, has been used as a substitute for vanillin. It may be detected by its low melting-point (about 67°) or by various other microchemical reactions, the most important one being the chlor-zinc-iodide test which gives brownish violet crystalline threads.

2. Benzoic acid has been used to dust inferior vanilla beans. It may be detected by its melting-point (120°), by its solubility in alkalis from which it crystallizes (on the slide) in feather forms when liberated by the addition of acids. Silver nitrate and sodium acetate gives a precipitate of brown needles. Benzoic acid is also microsublimable.

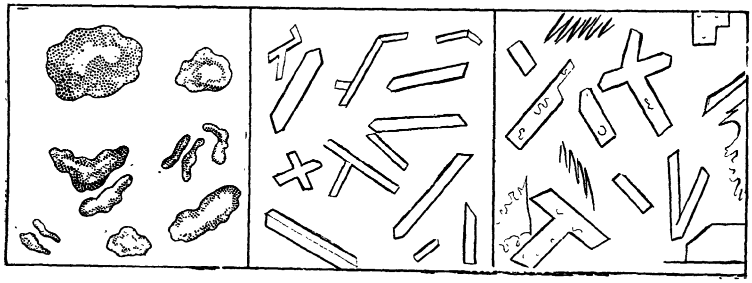
3. Acetanilid has been found as an adulterant of vanillin. It may be detected by warming the suspected crystals with alcoholic sodium hydroxide solution, adding a drop of chloroform and warming again, when, if acetanilid is present, the odor of phenylisocyanide may be perceived.

Cypripedium or Lady Slipper Root (U. S. P. 1863 to 1916; N. F. 1916 to 1936) is the dried rhizome and roots of *Cypripedium parviflorum* and *Cypripedium pubescens*, perennial herbs (Fig. 81) native in woods and thickets of the eastern and central United States and Canada.

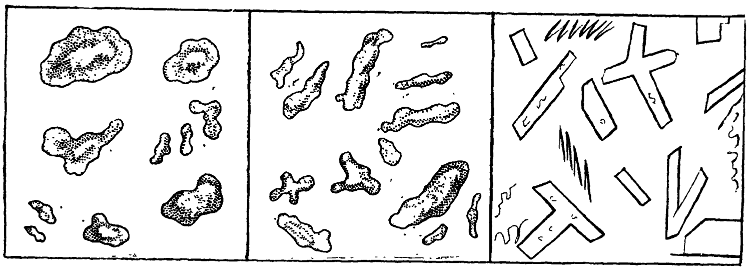
The rhizome is horizontal, somewhat tortuous and bent, 3 to 10 cm. long, 2 to 6 mm. in diameter; externally dark brown, annulate from scars of bud-scales, the upper surface with numerous large, sometimes repressed scars, the under and side portions with numerous roots and few root-scars.



(1) Crystals at ordinary temperature.



(2) Crystals at 67° to 69° C.



(3) Crystals at 80° to 82° C.

FIG. 80.—Examination of crystals by means of a thermo-stage. (1) Crystals at ordinary temperature. (2) Slide heated to 67° to 69° C., at which temperature coumarin melts, but the crystals of vanillin and benzoic acid remain normal. (3) Crystals heated to from 80° to 82° C., at which temperature vanillin melts.

The powder is yellowish or brownish, with calcium oxalate in raphides up to 70 microns in length; starch grains somewhat spheroidal, 2 to 14 microns in diameter, single or compound; tracheæ spiral, scalariform or with simple pores; sclerenchymatous fibers long, thin-walled; parenchyma thick-walled, with numerous simple pores.

Cypripedium contains a volatile oil; several resins; a bitter glycosidal principle; tannin; gallic acid; starch; calcium oxalate in the form of raphides; and ash about 6 per cent.

Cypripedium is occasionally used as a nerve stimulant and an antispasmodic. Average dose, 1 gm.

The rhizomes and roots of other species of *Cypripedium* possess properties analogous to the drug just described, and of these the following may be mentioned: *Cypripedium arietinum, C. candidum, C. hirsutum* and *C. acaule.*

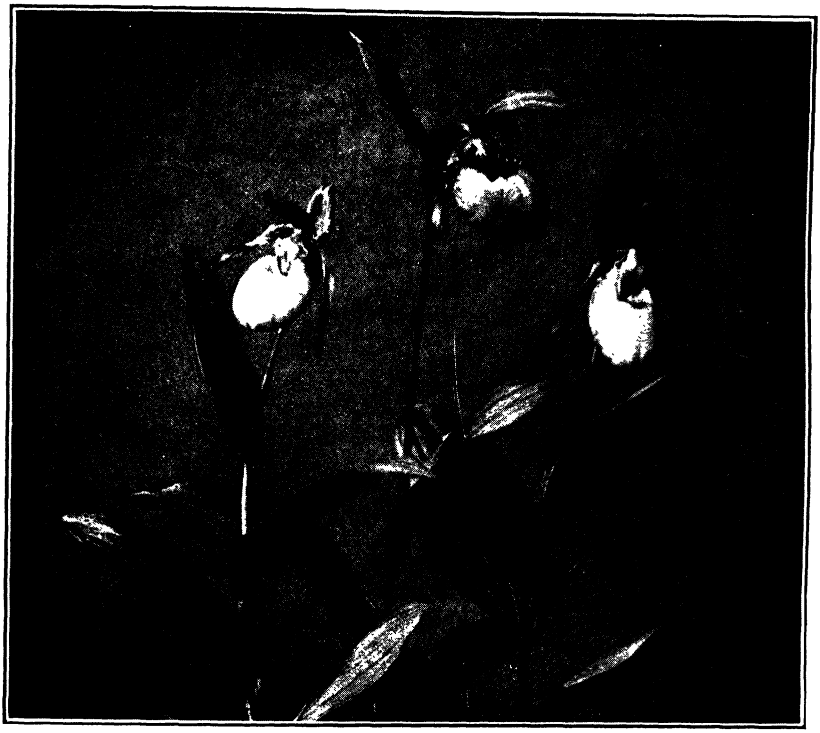


FIG. 81.—*Cypripedium pubescens.* Grown in slat house, Medicinal Plant Garden, University of Minnesota.

Salep or Tubera Salep (U. S. P. 1820 to 1831) is the fleshy tuberous roots of various species of *Orchis* and other allied genera. The tubers are collected from wild plants growing in Asia Minor, southern and southwestern Asia and are mostly shipped from Smyrna and Constantinople. At the flowering period the plant has 2 tubers, the one shriveled and from which the flowering plant is developed and the other young, firm and fleshy; only the latter ones are used. The tubers are scalded to destroy their vitality and to facilitate drying.

Salep is nearly globular, ovoid or somewhat ellipsoidal, more or less compressed; from 1 to 4 cm. in length and from 0.5 to 2 cm. in diameter; externally light yellowish or grayish brown, somewhat translucent, irregularly furrowed but otherwise nearly smooth, and occasionally with a small conical bud at the summit; hard and of a horny texture; inner surface with numerous scattered vascular bundles; inodorous and very mucilaginous (see Fig. 82).

Salep contains mucilage 48 per cent; starch 25 per cent; nitrogenous substances 5 per cent; sugar 1 per cent; ash from 1.5 to 4 per cent; and a trace of volatile oil.

Salep is a demulcent and a nutrient. Average dose, *ad libitum*.

Radix Palmæ Christi are the flattened 2- to 5-branched salep tubers, but these do not contain as much mucilage, though they are sometimes seen in the drug of commerce. The **Royal Salep** of Afghanistan is edible and is derived from *Allium macleanii*.

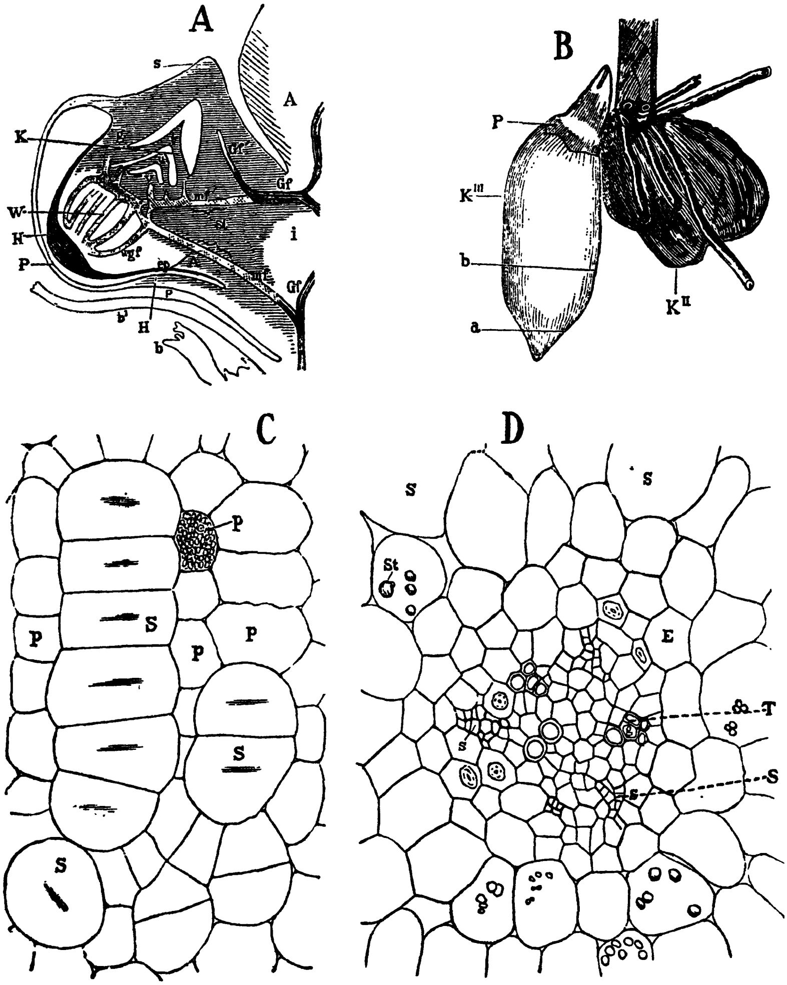


FIG. 82.—Salep. *A*, longitudinal section through the middle of a young tuberous root or tuber, showing portion of the old tuber (*A*) and the vascular bundles (*Gf*) connecting the two tubers, and the following parts of the young tuber: *s*, *b*, *u*, bud-scales; *w*, root; *h*, root cap, the whole being developed within the tissues of the axis of the mother tuber in a kind of sac (*P*). *B*, a pair of tubers, the one on the right being the parent tuber, and that on the left the young tuber from which the new plant will be developed in the coming season. The latter shows the remains of the sac-like scale (*P*) and through which the tuber has developed. *C*, longitudinal section through some of the parenchyma cells (*P*) showing the mucilage cells (*S*) with their small bundles of raphides. *D*, a radial vascular bundle showing the alternating plates of phloem (*S*) and tracheæ (*T*). (After Meyer.)

DICOTYLEDONEÆ–DICOTYLEDONS

The plants of this class present the highest development in the plant kingdom and comprise about three-fourths of the living Angiosperms. They are characterized by having two seed-leaves or cotyledons in the embryo. The foliage leaves are usually bilateral and reticulately veined. The flowers are usually tetramerous or pentamerous. The roots and the stems are characterized by a distinct cambium, therefore secondary growth of the wood and the bark is usual and a secondary cork by means of a phellogen is not unusual. The stems of secondary growth show a ring of open collateral fibrovascular bundles radially arranged about a central pith. The class includes herbs, shrubs and trees.

PIPERACEÆ, OR PEPPER FAMILY

Most of the members of this family are herbs and shrubs which have secretory cells in the stems and leaves. In the latter they are conspicuous as small transparent dots. The species of *Piper*, comprising more than one-half of the members of the family, are mostly shrubs having swollen nodes and fleshy spikes of flowers. The leaves are opposite and bifacial, having stomata on the lower surface only. Non-glandular and glandular hairs may be present. The fruit is a drupe, enclosing a seed containing endosperm and abundant perisperm.

CUBEB

Cubeb or Cubeb-Berries (U. S. P. 1820 to 1936; N. F. 1936 to date) is the dried, nearly full-grown, unripe fruit of *Piper cubeba* Linné filius. The plant is a woody climber indigenous to Borneo, Java and Sumatra, where it is also cultivated, being trained upon the trees used as shade for coffee trees. The specific name *cubeba* is the native term for the plant. The fruit is gathered when nearly full-grown but still green, and carefully dried in the sun, the commercial supplies being shipped from Batavia and Singapore. Arabian physicians of the ninth and tenth centuries were acquainted with the medicinal properties of cubeb. The fruits were used as a spice in Europe as early as the eleventh century, but did not regain medicinal usage until the beginning of the nineteenth century. Since 1818 they have been included in most pharmacopœias.

Description, Structure and Powder.—See Figures 83 and 84 and the National Formulary.

Constituents.—By steam distillation cubeb yields 10 to 18 per cent of **Oil of Cubeb** (U. S. P. 1842 to 1926), a volatile oil consisting chiefly of terpenes and sesquiterpenes and a sesquiterpene hydrate known as cubeb camphor. Cubeb also contains 2.5 to 3.5 per cent of resins; 1 to 3.5 per cent of cubebic acid; 0.4 to 3 per cent of a bitter crystalline principle, cubebin; 1 per cent of fixed oil; 8 per cent of gum; starch; and about 6 per cent of ash. Cubebin and cubebic acid are colored red by sulfuric acid.

Standards and Tests.—Cubeb contains not more than 10 per cent of its shriveled fruit or 5 per cent of its stems, not more than 2 per cent of other foreign organic matter, and yields not less than 13 per cent of volatile cubeb oil, and not more than 2 per cent of acid-insoluble ash. Cubeb, powdered or crushed, mixed with sulfuric acid produces a crimson-red coloration of the acid.

Uses and Dose.—Cubeb is a diuretic, an antiseptic, a stimulating expectorant and a carminative. Average dose, 2 gm.

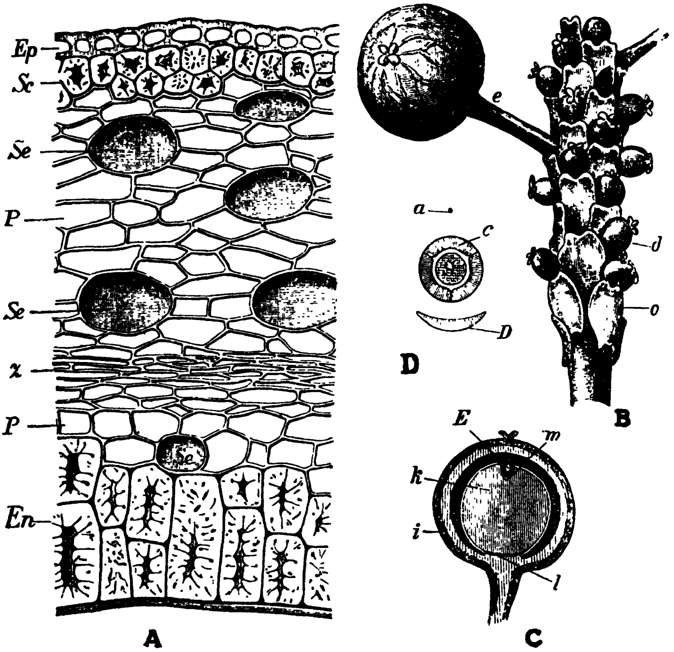


Fig. 83.—Cubeb: *A*, transverse section of the pericarp showing epidermis (*Ep*), stone cells (*Sc*), oil cells (*Se*), parenchyma (*P*), collapsed parenchyma tissue (X), endocarp (*En*) composed of stone cells. *B*, spike showing bracts (*a*), young sessile fruits (*d*), and a mature fruit with long pedicel (*e*). *C*, longitudinal section of mature fruit showing pericarp (*i*), union (*l*) of seed and pericarp, large perisperm (*k*), small endosperm (*m*), which surrounds the embryo (*E*). *D*, flower diagram showing the position of the flower in reference to the rachis (*a*), bract (*D*) and pericarp (*c*) which surrounds the ovule (*S*). (After Meyer.)

Adulterants and Allied Plants.—The fruits of other species of *Piper*, particularly *P. ribesoides*, sometimes find their way into market; *Piper cubeba* var. *rinoe badak*, exhibits stone cells throughout the parenchyma. These fruits are grayish in color, larger, with stalks, and are somewhat bitter. The sulfuric acid test, together with anatomical differences, serve to distinguish these and other allied species from genuine cubeb.

A number of other species of *Piper* yield fruits resembling cubeb, as *P. clusii*, of West Africa; *P. borbonense*, of Bourbon; *P. sumatranum* and *P. pedicellosum*, of Indo-China.

The fruit of *Toddalia lanceolata* (Fam. *Rutaceæ*) is used in Africa in place of cubeb. The fruits of *Litsea citrata* have been sold as False Cubeb, and those of *Litsea cubeba* (Fam. *Lauraceæ*) are substituted for cubeb in Cochin China.

Not infrequently a considerable amount of the rachis is present and this contains a relatively small amount of the active principles. The rachis may be detected in the powder by the presence of long, strongly lignified fibers having a broad lumen.

Black Pepper (U. S. P. 1820 to 1926; N. F. 1926 to 1936) is the dried, full-grown but unripe fruit of *Piper nigrum* Linné. The plant is a woody, perennial climber, indigenous to Cochin China and various parts of India, and cultivated in the East Indies, West Indies and other tropical countries. The commercial supplies come mostly from Batavia and Singapore. The latter furnishes the best grade of black pepper and, as it is fire-dried, it possesses a somewhat smoky odor and taste.

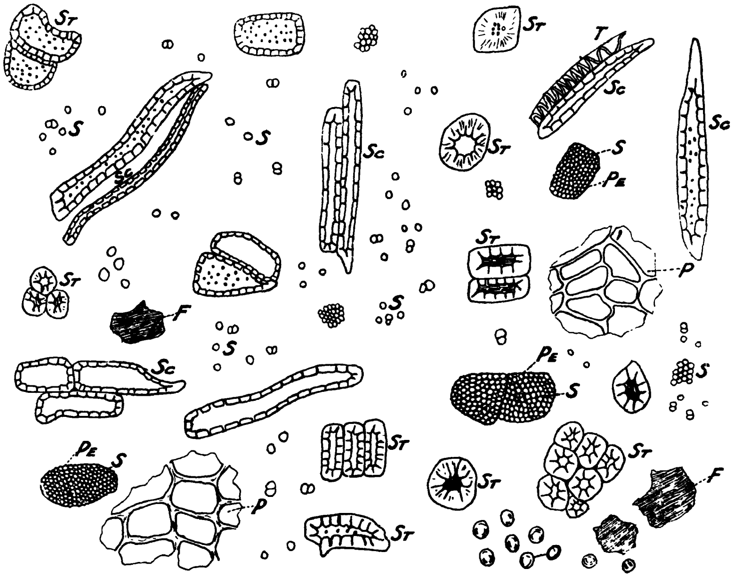


FIG. 84.—Powdered Cubeb. (*St*) stone cells, single or in isolated groups, nearly isodiametric, thick-walled, with numerous simple pores, and colorless or light yellow contents; (*T*) spiral tracheæ and sclerenchymatous fibers (*Sc*) few, the latter short, thick-walled, and strongly lignified; parenchymatous cells (*P* and *Pe*) with reddish brown tannin masses (*F*); oil-secretion cells with suberized walls; oil globules (*O*) numerous; starch grains (*S*) numerous, single or compound, the individual grains 2 to 12 microns in diameter. (Drawing by Hogstad.)

Black Pepper was known to Theophrastus and other ancient writers. It was introduced into Europe about the year 1000 and was the most important spice then known.

Pepper vines are trained on poles and trellises, the fruits being picked when the lowest ones on the rachis begin to turn red, and are dried in the sun or with artificial heat.

DESCRIPTION AND STRUCTURE.—See Figure 85.

Powdered black pepper is grayish brown; aromatic in odor; aromatic and pungent in taste; with numerous stone cells; much starch compacted into parenchyma cells; parenchyma fragments containing oil-secretion cells with suberized walls, cells with reddish brown amorphous contents, and other cells with needle crystals of piperine. The subepidermal stone cells are nearly isodiametric with uniformally thickened, porous walls and containing yellowish brown tannin masses which give a blue color with ferric ammonium sulfate T.S.; the endodermal stone cells have thin outer walls and thickened radial and inner walls. The starch grains are angular or spheroidal and up to 6 microns in diameter.

Black pepper contains 1 to 2 per cent of volatile oil containing dipentene, phellandrene and a peculiar terpene; the alkaloid piperine, 4.5 to 8 per cent; piperidine, a colorless liquid alkaloid, which is a hydrolytic product of piperine; a pungent resin, chavicin; starch; tannin; about 10 per cent of proteins; and 5 per cent of ash.

Piperine (U. S. P. 1882 to 1916), one of the earliest alkaloids isolated (Oerstedt, 1819), is fairly soluble in alcohol, chloroform, benzol and ether but only slightly soluble in water. It crystallizes in monoclinic prisms melting at 128° C. Piperine is the piperic acid ester of piperidine, and treatment with KOH will readily hydrolyze it into piperidine and the potassium salt of piperic acid.

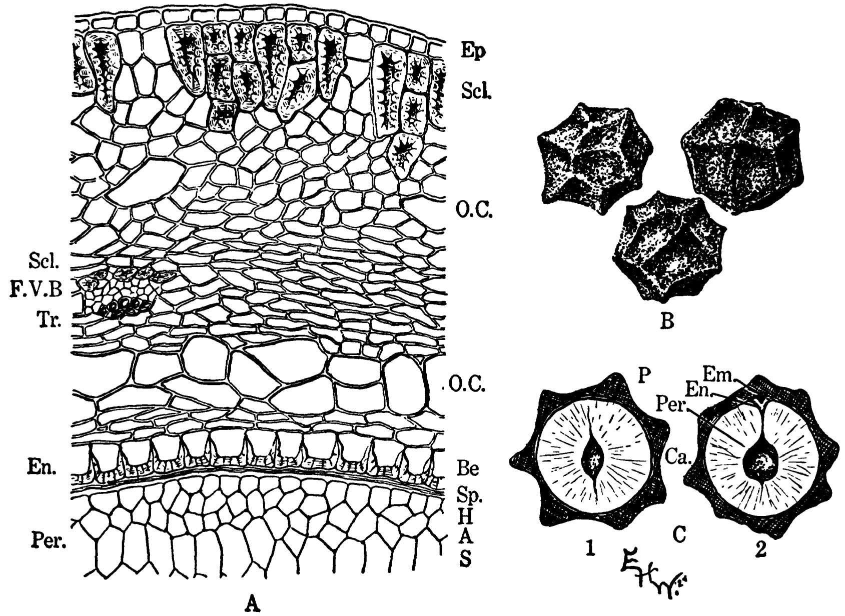


Fig. 85.—Black Pepper. *B*, commercial whole fruit 3.5 to 6 mm. in diameter, blackish brown and coarsely reticulate. *C*, lens view of sections of whole fruit; (*1*) transverse and (*2*) longitudinal: *P*, pericarp; *Per*, perisperm; *En*, endosperm; *Em*, embryo. *A*, transverse section of the pericarp: *Ep*, epidermis; *Scl*, sclerenchyma; *OC*, oil cells; *FVB*, fibrovascular bundle; *Tr*, tracheæ; *En*, endodermis of beaker cells; *Sp*, spermoderm; *Per*, perisperm; *H*, hyaline layer; *A*, aleurone layer; *S*, starch layer. (Drawings by E. H. Wirth.)

To demonstrate piperine, mount powdered black pepper in alcohol, cover with a cover-glass, and add a drop of water; long needles of piperine will readily separate usually near the edge of the cover-glass or, if crystallization proceeds slowly, prismatic crystals may be obtained (see Fig. 86). Rosenthaler identifies piperine by mounting the powder in hydrochloric acid to which a small crystal of cadmium acetate has been added; sheaves of yellow needles consisting of the piperine-cadmium compound will separate (see Fig. 87).

Black pepper yields not less than 6.75 per cent of non-volatile ether extract, not more than 1.5 per cent of ash insoluble in hydrochloric acid, not more than 15 per cent of crude fiber, and not more than 2 per cent of stems or other foreign matter. The aromatic principles are found mostly in the pericarp, while the pungency is distributed throughout the seed; the more pungent and delicately aromatic peppers are preferred.

Piper is used as a condiment. It is a stimulant, an irritant, a tonic and a febrifuge. Average dose, 0.5 gm.

Black pepper in U. S. commerce has been extensively adulterated until the National Pure Food and Drugs Act became widely enforced. Since then such adulteration has gradually decreased to practically nil. Former adulterations included pepper hulls, representing the broken pericarp of the fruit obtained in the preparation of White Pepper; capsicum to increase pungency; starchy

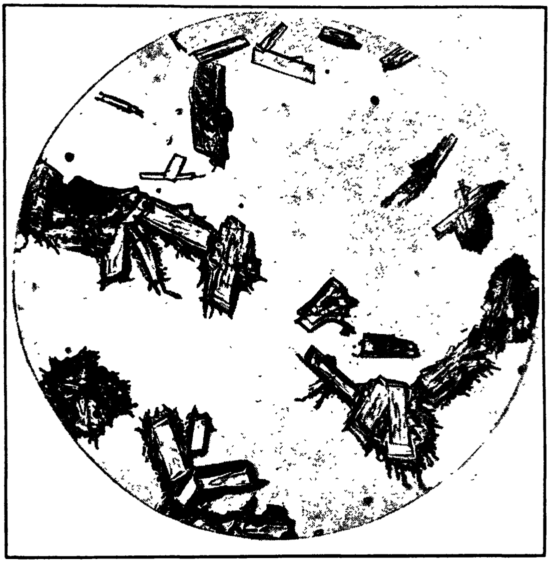


Fig. 86.—Piperine. (Photo by Adamson.)

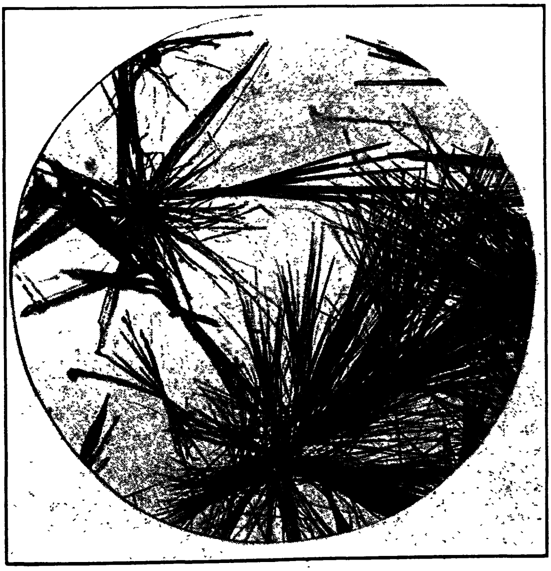


Fig. 87.—Piperine-cadmium compound. (Photo by Adamson.)

products; stone cell products, such as drupe pits, nut shells, etc.; woody products (sawdusts); and inorganic materials (chalk, gypsum, etc.).

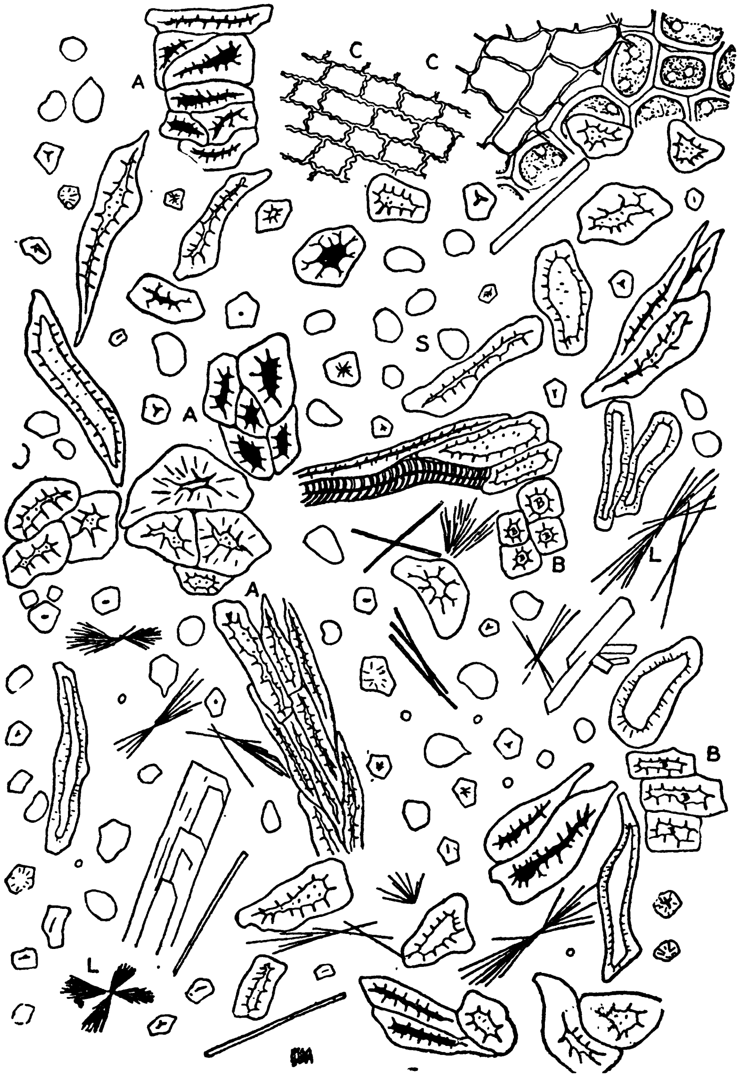


FIG. 88.—A mixture sold as ground black pepper but devoid of black pepper: *A*, stone cells of olive endocarp; *S*, corn and wheat starch grains; *B*, stone cells of pepper hulls; *C*, fragments of seed coat and pericarp of cayenne pepper; *L*, crystals of calcium sulfate which separate on mounting the specimen in 25 per cent sulfuric acid.

Among the black pepper substitutes are: the fruit of *Embelia ribes* (Fam. *Myrsinaceæ*), a small tree of India; of *Polyadenia pipericarpa* (Fam. *Lauraceæ*) of Sumatra and the fruits of a number of species of *Xylopia* (Fam. *Anonaceæ*) containing aromatic and bitter principles; some of these fruits are used like pepper for condiment purposes; among them are *X. æthiopica* of Uadai (Africa), and *X. grandiflora*, *X. sericea* and *X. frutescens* of Brazil. *X. aromatica* yields the **Guinea Pepper.**

White Pepper consists of the fruits of *Piper nigrum* which have ripened and from which the outer portion of the pericarp has been separated after the fruits have soaked in salt water or lime water. White pepper is globular and yellowish gray in color. Removal of the outer pericarp exposes the fibrovascular bundles, about 15 in number, which appear as ridges on the outer surface extending from

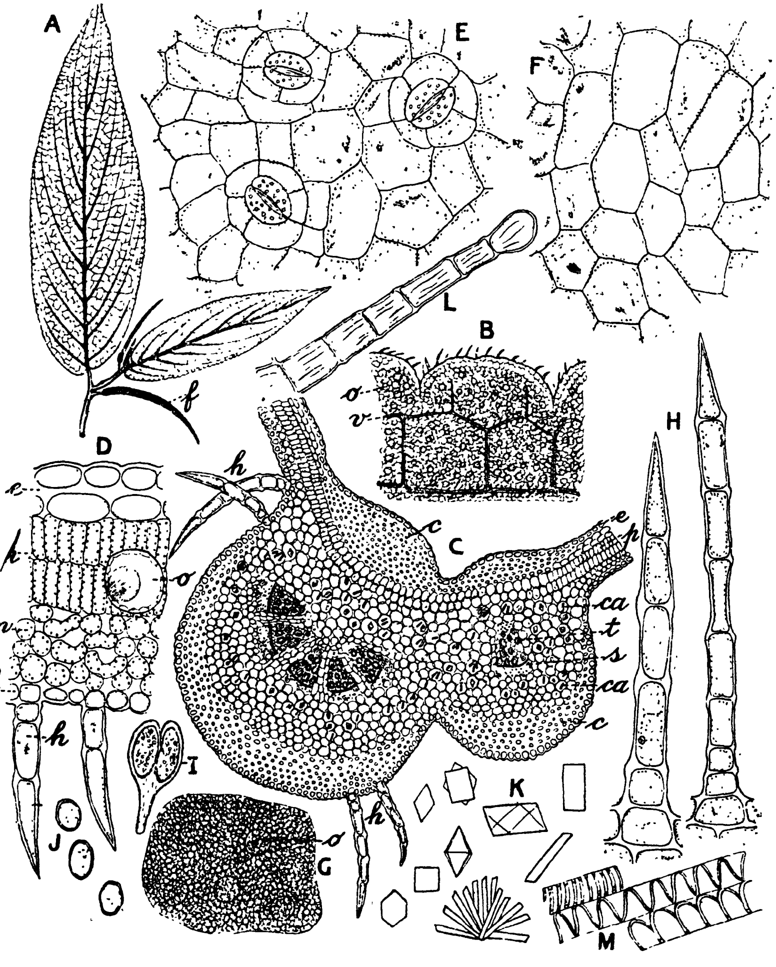


FIG. 89.—Matico. *A*, branch with leaves and flower spikes (*f*); *B*, section of leaf showing one of the truncate teeth, fibrovascular bundle (*v*), oil-secretion reservoirs (*o*); *C*, transverse section of leaf near two veins, showing upper epidermis and a hypodermis of several layers (*e*), palisade cells (*p*), tracheæ (*t*), sieve (*s*), collenchyma (*c*), loose parenchyma containing crystals of calcium oxalate (*ca*), hairs (*h*); *D*, transverse section of leaf showing in addition an oil-secretion reservoir (*o*); *E*, portion of lower epidermis showing three stomata; *F*, portion of upper epidermis; *G*, portion of leaf showing the glandular punctate character due to the oil secretion reservoirs (*o*); *H*, non-glandular hairs 200 to 1000 microns in length, and with walls 2 to 4 microns thick; *I*, stamen; *J*, pollen grains, which are about 10 microns in diameter; *K*, prisms of calcium oxalate; *L*, a hair from the perianth; *M*, tracheæ from the stem with spiral and annular markings.

base to apex. Ground white pepper is practically devoid of the larger isodiametric stone cells of the outer pericarp. It is less pungent and aromatic than black pepper, but due to its more delicate flavor is highly esteemed as a condiment.

Long Pepper (U. S. P. 1830, N. Y. ed.) is the fruit of *Piper longum*, a shrub indigenous to the Malay Archipelago and consists of the entire spikes of the immature fruit. The spikes are cylindrical, from 2.5 to 4 cm. long, about 5 mm. thick, of dark grayish color, and the drupes are less aromatic and pungent than black pepper. Oil cells in the sarcocarp and "beaker cells" in the endocarp are absent, and the starch grains of the perisperm are from 2 to 10 microns in diameter. Long pepper yields about 4 per cent of piperine and about 1 per cent of a volatile oil with a pungent taste resembling that of oil of pepper, but with an odor resembling that of ginger.

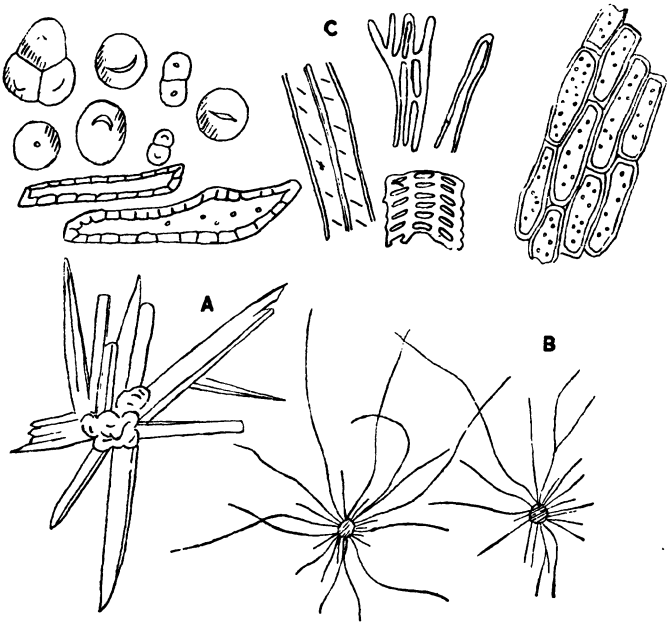


FIG. 90.—*A*, crystals of methysticin obtained on treatment of sections or the powder of Kava with alcohol, the crystals being of a light yellow color, attaining a length of 160 microns and becoming violet-red on the addition of sulfuric acid. *B*, crystals of methysticinic acid obtained upon heating a small quantity of the powder with one or two drops of a solution of potassium hydroxide and adding dilute alcohol and allowing the slide to stand for twenty-four hours. *C*, elements of the powder, including starch grains, sclerenchyma cells, fragments of tracheal tubes and slightly lignified, porous parenchyma cells from the medullary rays. (After Tunmann.)

Long pepper is also obtained from *Piper officinarum*, of Java, India and the Philippine Islands; *Piper sylvaticum*, of eastern India; *Chavica officinarum*, of the West Indies; and *Peperomia acuminata*, of Peru.

Matico (U. S. P. 1863 to 1916; N. F. 1916 to 1936) consists of the dried leaves of *Piper angustifolium*, a shrub indigenous to Peru and Bolivia. The specific name *angustifolium* means "narrow-leaf."

Matico usually occurs in large, compressed, matted masses; the leaves are short petiolate, oblong-lanceolate, 10 to 20 cm. long and 2 to 5 cm. broad (see Fig. 89).

Matico contains a volatile oil, the stearopten matico camphor, an acrid resin, a bitter principle and arthantic acid.

Matico is a stimulant and an antiseptic to the urinary tract. It is an astringent, a styptic, and vulnerary. Average dose, 4 gm.

Kava or Methysticum (N. F. 1916 to 1936) is the rhizome and roots of *Piper methysticum*, a plant indigenous to and cultivated in the South Sea Islands from Hawaii to the East Indies.

The drug occurs in irregular, transverse and longitudinal pieces, varying from 3 to 20 cm. in length and 1 to 12 cm. in diameter. These are light yellowish or grayish brown, longitudinally wrinkled and with large circular root-scars. The inner surface is light yellowish brown, with a large pith, a distinctly radiate xylem and occasionally a thin bark. A drop of sulfuric acid applied to the surface produces a deep cherry-red color. The odor of the drug is slight and the taste is sweetish and pungent, followed by a slight numbness. Pieces of the stem are more woody and have a hollow pith.

Kava contains about 5.3 per cent of resin, and the active constituents, methysticin, a derivative of piperic acid, and ω-methysticin. Methysticin may be identified by mounting powdered kava in alcohol; after partial evaporation of the solvent, prismatic needles appear at the edge of the cover-glass. The crystals polarize red-violet to yellow and dissolve with a purple color in H_2SO_4. Methysticin may also be obtained from kava powder by microsublimation, the result being much better if the powder is first treated with dilute H_2SO_4, emulsin or saliva.

Kava is a mild diuretic, an expectorant and a genito-urinary stimulant and antiseptic. Average dose, 1 gm.

SALICACEÆ, OR WILLOW FAMILY

This family consists of two genera, viz.: *Salix* and *Populus*, with about 160 species of the former and 30 of the latter. The willows usually grow in wet ground and are extensively cultivated not only for ornamental purposes but for their economic uses, and occasionally for drying out damp ground, especially where the conditions are unsanitary. The twigs are used in the making of baskets, the wood furnishes a charcoal which is employed in medicine and in making crayons and gunpowder, and the bark yields salicin. The "pussy willow" (*Salix discolor*) is a small tree rather common in low meadows and river banks and is marked by thick cylindrical aments, the scales being copiously clothed with long glossy hair. The poplars are planted because of their rapid growth as shade trees, and to serve as windbreaks, especially in the western States. The wood is largely used in making paper, cardboard, etc. The balsam poplar or tacamahac (*Populus balsamifera*) and the balm of Gilead (*P. candicans*) are well-known trees of the United States, distinguished by their large resiniferous buds, used medicinally.

Salix or Willow Bark (U. S. P. 1820 to 1894) is the bark of *Salix alba*, a noble tree indigenous to Europe and naturalized in the northern United States and Canada. The generic name *Salix* is an ancient Latin term; *alba* is the Latin for white. In the spring of the year, the bark is stripped from the two- or three-year-old branches and quickly dried. If from more mature branches or from the trunk, it is frequently deprived of the periderm.

The bark contains tannin, about 13 per cent; salicin, in variable amounts about as follows: outer bark, 2.5 per cent; middle bark, 5.8 per cent; innermost layers, 11.3 per cent; bark collected in spring, 7.38 per cent; and that gathered in the fall, 6.66 per cent.

Willow bark is used as an astringent.

The bark of the black willow (*Salix nigra*) is used to some extent in this country. The tree is rather common in the United States, growing almost everywhere except in California. The bark of *Salix discolor* contains, in addition to salicin, the glucoside of metahydroxybenzaldehyde, salinigrin.

Poplar Bark (as a source of Salicin U. S. P. 1895 to 1936) is the bark of the white or silver poplar, also known as the great aspen or abele (*Populus alba*).

The drug consists of quills or flat pieces, varying in length and from 0.5 to 3 mm. in thickness; outer surface greenish white, smooth and with numerous lenticels; inner surface light brown and longitudinally striated; fracture short-fibrous; odor slight; taste bitter and astringent.

The bark contains, in addition to salicin, the glucoside populin or benzoylsalicin, which forms needle-shaped crystals, having a somewhat sweetish and acid taste and yielding upon hydrolysis saligenin (salicylic alcohol) and benzoic acid.

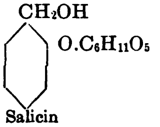
Poplar Bark is used as a tonic and a febrifuge.

Salicin (U. S. P. 1882 to 1936; N. F. 1936 to date) is a glucoside obtained from several species of *Salix* and *Populus*. It occurs in colorless shining needles or prisms melting at about 200° C. Salicin is soluble in water and alcohol but insoluble in chloroform and ether.

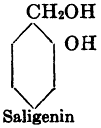
Most willow and poplar barks yield salicin, but the principal commercial source seems to be *Salix purpurea* and *Salix fragilis*, which are grown to a considerable extent in Belgium and are used for making baskets. They yield a thin reddish colored bark known as "rood schors." Salicin is usually obtained by macerating the bark in hot water for several hours; then filtering, concentrating in vacuum, treating with lime, and then with basic lead acetate to remove tannin. After removal of the excess lead the liquid is further concentrated until crystallization takes place. The crystals are separated, redissolved, the solution filtered through animal charcoal and recrystallized.

PROPERTIES:

1. Salicin is hydrolyzed into *b*-glucose and saligenin by emulsin.



Salicin



Saligenin

2. Saligenin may be oxidized ($K_2Cr_2O_7$ + H_2SO_4) into salicylic aldehyde having a characteristic odor.

3. Salicin gives a brown color with ferric chloride T.S. After hydrolysis the saligenin formed gives a violet color with ferric chloride T.S., due to the free OH group. Likewise salicin does not give the Fehling reaction but after hydrolysis the presence of glucose may be demonstrated by the reduction of the alkaline copper tartrate. Both these reactions serve to demonstrate the glucosidal properties of salicin.

4. Salicin gives a red color upon treatment with sulfuric acid which disappears upon the addition of water. This test has given some success in the localization of salicin in tissues.

USES AND DOSE.—Salicin is probably decomposed into salicylic acid in the human system. Its action resembles that of salicylic acid very closely. It is a bitter tonic, an antiperiodic and an antirheumatic. Average dose, 1 gm.

POPLAR BUD

Poplar Bud (N. F. 1916 to date) is the air-dried, closed, winter leaf-bud of *Populus candicans* Aiton, known in commerce as Balm of Gilead buds or of *Populus Tacamahacca* Miller (*Populus balsamifera* Linné), known in commerce as Balsam Poplar Buds. The trees yielding poplar bud are found in the northern United States and Canada. They occasionally reach a height of 100 feet and a trunk diameter of 6 feet. *Populus* is the ancient Latin name of the poplar, from *arbor populi,* meaning "the people's tree," because it was used to decorate public walks; *balsamifera* means bearing fragrant balsam; *candicans* is from the Latin *candicare,* meaning whitish, referring to the color of the bark; and *Tacamahacca* is from the Spanish literally meaning "stinking pot tree." The leaf-buds are collected in the spring before they open. The buds of

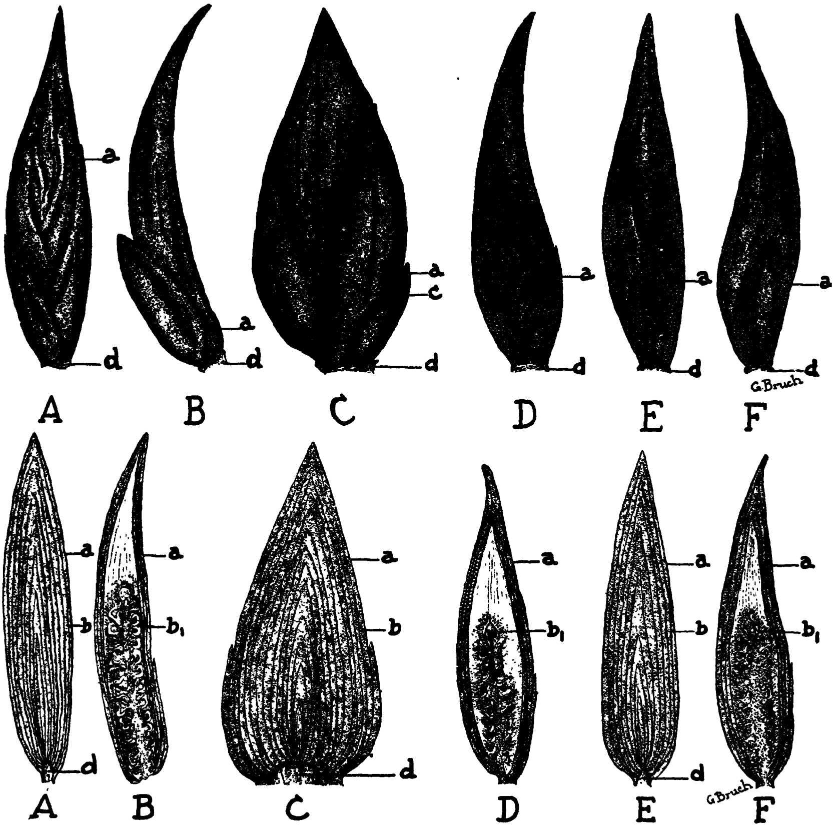


Fig. 91.—Whole Poplar Buds (above); and median longitudinal section of Poplar Buds (below): *A*, *Populus nigra* leaf-bud; *B*, *P. nigra* flower-bud; *C*, *Populus candicans* leaf-bud; *D*, *P. candicans* flower-bud; *E*, *Populus balsamifera* leaf-bud; *F*, *P. balsamifera* flower-bud; *a*, outer scale; *b*, resinous exudation; *b′*, catkin of flowers; *c*, second scale; *d*, stem-scar. (Drawings by G. Bruch.)

the black poplar were known to Dioscorides and Theophrastus, but seem not to have been used internally as expectorants until toward the end of the nineteenth century.

Description and Structure.—See Figures 91, 92, 93, 94 and the National Formulary.

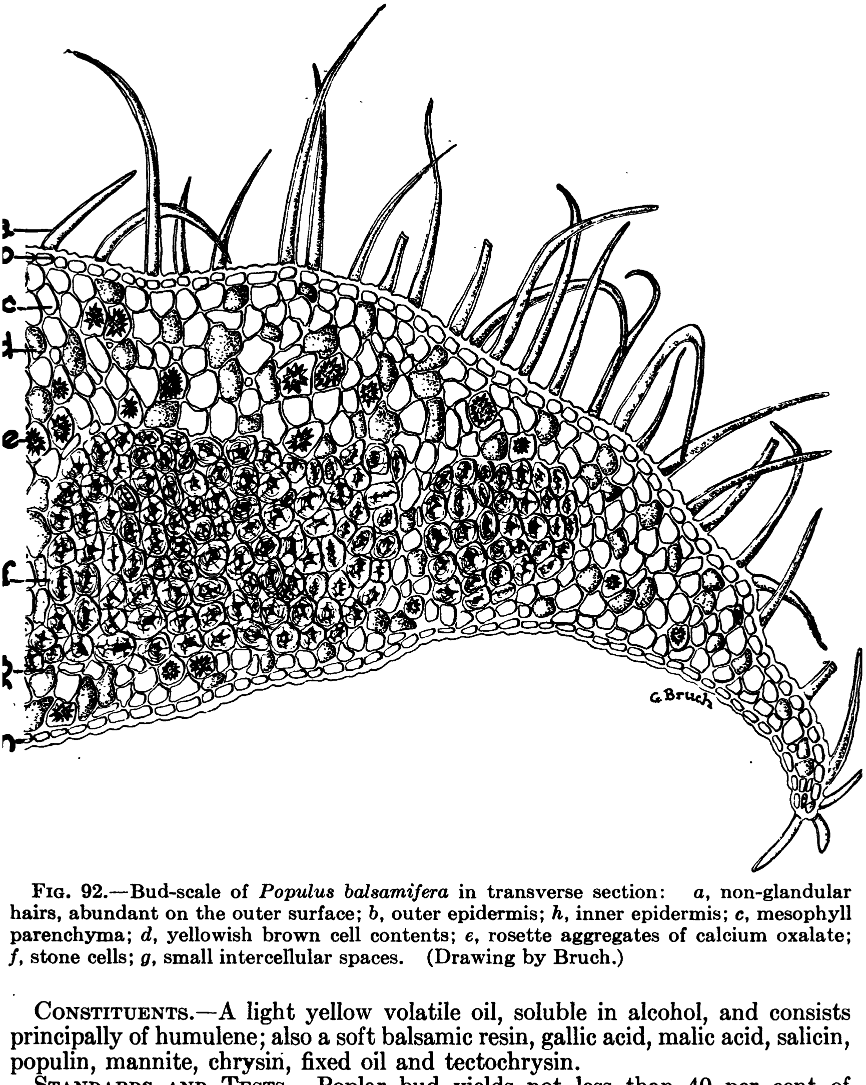


Fig. 92.—Bud-scale of *Populus balsamifera* in transverse section: *a*, non-glandular hairs, abundant on the outer surface; *b*, outer epidermis; *h*, inner epidermis; *c*, mesophyll parenchyma; *d*, yellowish brown cell contents; *e*, rosette aggregates of calcium oxalate; *f*, stone cells; *g*, small intercellular spaces. (Drawing by Bruch.)

Constituents.—A light yellow volatile oil, soluble in alcohol, and consists principally of humulene; also a soft balsamic resin, gallic acid, malic acid, salicin, populin, mannite, chrysin, fixed oil and tectochrysin.

Standards and Tests.—Poplar bud yields not less than 40 per cent of anhydrous alcohol-soluble extractive, not more than 1 per cent of acid-insoluble ash, and contains not more than 16 per cent of flower-buds from the plants yielding poplar bud.

Uses and Dose.—Poplar bud is employed as a stimulant and expectorant. Average dose, 4 gm.

Adulterants.—The buds of the fir (*Abies balsamea*, Fam. *Pinaceæ*) furnish an article known as **False Balm of Gilead Buds.** They are very aromatic and resinous and contain, besides tannin, a bitter glucoside, picein.

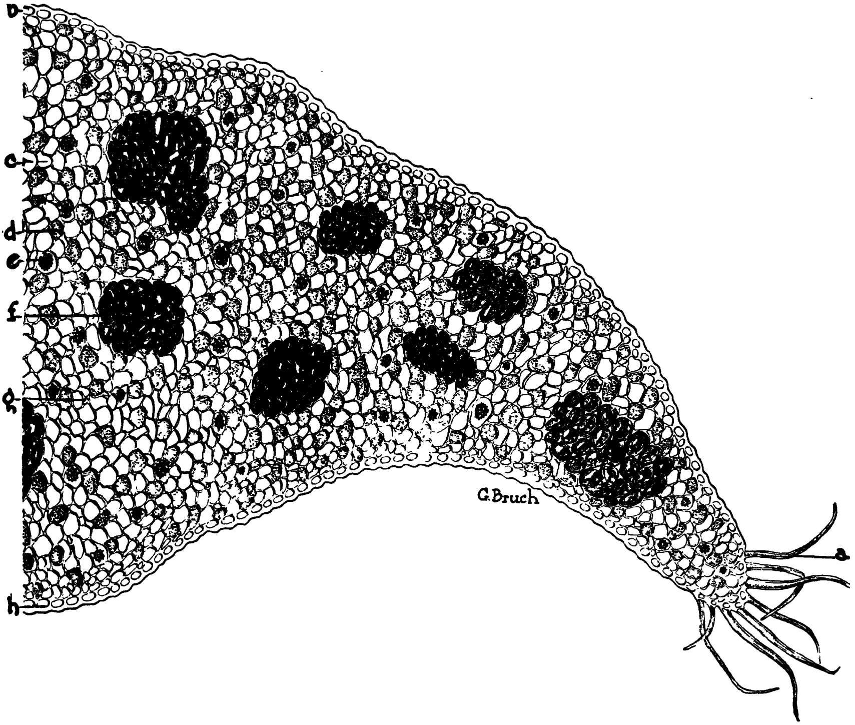


FIG. 93.—Bud-scale of *P. candicans* in transverse section: *a*, non-glandular hairs, found at the margin only; *b*, outer epidermis; *h*, inner epidermis; *c*, mesophyll parenchyma; *d*, yellowish brown cell contents; *e*, calcium oxalate rosettes; *f*, stone cells; *g*, small intercellular spaces. (Drawing by Bruch.)

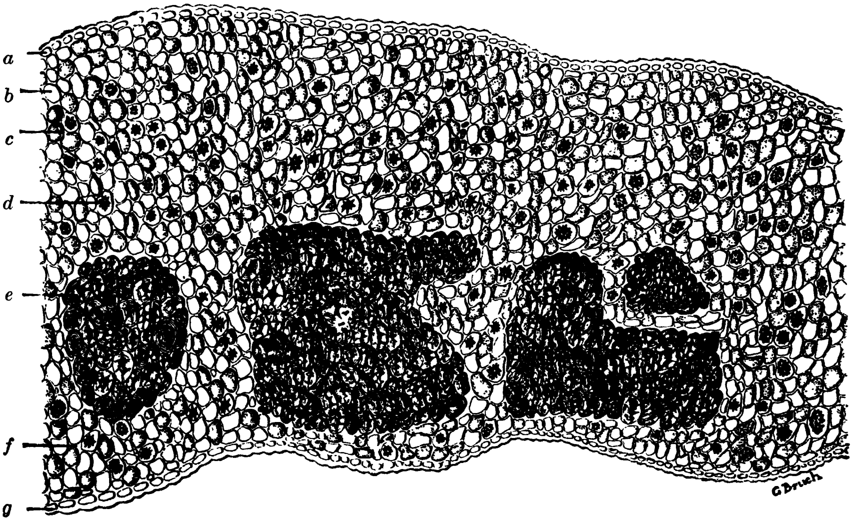


FIG. 94.—Bud-scale of *P. nigra* in transverse section: non-glandular hairs wanting. *a*, outer epidermis; *g*, inner epidermis; *b*, mesophyll parenchyma cells; *c*, yellowish brown cell contents; *d*, rosette of calcium oxalate crystals; *e*, stone cells; *f*, intercellular space. (Drawing by Bruch.)

Black Poplar (N. F. 1916 to 1936) consists of the buds of *Populus nigra*. They show fewer and shorter outer scales and exhibit no hairs. Buds of other *Populus* species are rarely found.

CHARCOAL

Activated Charcoal (U. S. P. 1936 to date) is the residue from the destructive distillation of various organic materials, treated to increase its adsorptive power.

It is a fine, black, odorless and tasteless powder, free from gritty matter. Activated charcoal should yield not more than 4 per cent of ash and not more than 3.5 per cent of acid-soluble substances. Carbonization must be complete as detected by the coloring of sodium hydroxide solution. It must be neutral to litmus and free from chlorides, sulfates, sulfides, cyanogen compounds and heavy metals, within the limits of the Pharmacopœia. The U. S. Pharmacopœia also makes standards for the adsorptive power of activated charcoal against strychnine sulfate, methylene blue and hydrogen sulfide.

Wood Charcoal (U. S. P. 1820 to 1936) is prepared by the destructive distillation of wood from the following genera: *Salix*, *Populus*, *Quercus* or *Corylus*. Two methods are employed for the production of charcoal: the older or "stack" method consists of piling the chips of wood in a conical pile or stack, covering this with earth and sod; leaving several openings at the bottom and one at the top; and igniting the bottom of the stack, after which the lower openings are closed; the newer method consists of burning the wood without access of air in cast iron retorts. The yield varies from 15 to 25 per cent and the charcoal made from willow or poplar is preferred. When used for medicinal purposes, wood charcoal must meet the requirements of activated charcoal.

Purified Animal Charcoal (U. S. P. 1842 to 1916; N. F. 1926 to date) is made by the destructive distillation of bone, and purified by boiling with hydrochloric acid. Its properties and standards are similar to those of activated charcoal.

MYRICACEÆ, OR SWEET GALE FAMILY

This is a family consisting of a single genus, of which the wax myrtle, or bayberry, *Myrica cerifera*, is the best known species.

Myrica, Bayberry Bark or Wax Myrtle Bark (N. F. 1916 to 1936) is the bark of the root of *Myrica cerifera*, a small shrub growing in sandy soil near the sea coast from New Jersey to Florida. It produces diminutive clusters of small wax-covered berries, and the wax, when melted off and mixed with tallow, is used to form candles. The bark is separated from the roots gathered late in the fall, cleaned and dried.

The bark occurs in strips or quills with a reddish brown outer surface and a dark brown, fine striate inner surface. The fracture is short and mealy; the odor distinct and aromatic; the taste slightly bitter and astringent, becoming pungent and acrid.

For structure see Figure 95.

The powdered drug is light reddish brown and sternutatory, with numerous single or compound starch grains up to 12 microns in length, and monoclinic prisms or rosette aggregates of calcium oxalate. Bast fibers, stone cells and crystal fibers with strongly lignified, porous walls are present; as also cork cells with thick, lignified or brownish walls and occasional woody fragments showing tracheæ with bordered pores.

Myrica contains a trace of volatile oil; two resins; myricinic acid; from 2.5 to 3.5 per cent of tannic acid; a trace of gallic acid, of sugar, and of mucilage.

Myrica is an astringent and a tonic. Average dose, 0.5 gm.

ALLIED PRODUCTS.—The bark of the root of *Myrica carolinensis*, Northern Bayberry, also is found in the drug. The rhizome and leaves of the **Sweet Fern** (*Myrica asplenifolia*), and the leaves of the **Sweet Gale** (*Myrica gale*), are aromatic astringents occasionally used in medicine.

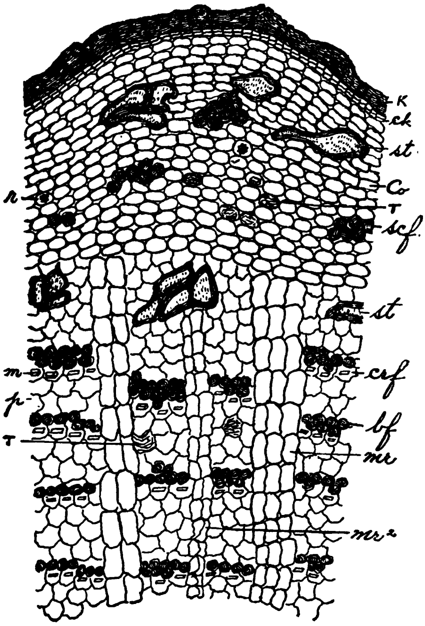


FIG. 95.—Transverse section of root bark of *Myrica cerifera*, showing cork (*K*); cork cambium (*ck*); cortex (*Co*); tannin cells (*T*); stone cells (*st*); sclerenchyma fibers (*scf*); rosette crystals of calcium oxalate (*r*); monoclinic prisms of calcium oxalate (*m*); phloem (*p*); bast fibers (*bf*); primary medullary ray (*mr*); secondary medullary ray (*mr*²); and crystal fibers (*crf*). (After H. W. Youngken.)

JUGLANDACEÆ, OR WALNUT FAMILY

This is a small family of six genera, the most important of which are *Juglans* and *Hicoria*. These trees yield useful woods, the barks are used in tanning and dyeing, and the fruits are edible. *Hicoria pecan* bears the **pecan nut** found in the southern states; *H. ovata*, a large and handsome tree, known as shag-bark hickory, is the chief source of the **hickory nuts** of the market. There are six other common species of *Hicoria* which are indigenous to the United States and Canada, and all yield edible nuts.

The hulls (epicarp and mesocarp) of the English walnut, *Juglans regia*, have been used as an astringent, and the ground **nut shells** (endocarp) of this, as well as the other walnuts and hickory nuts, have been found as adulterants of spices.

Butternut Bark (U. S. P. 1820 to 1905; N. F. 1916 to 1936) is the inner bark of the root of *Juglans cinerea*, a tree growing in rich moist soil in the eastern and central United States. *Juglans* is a contraction of "Jovis glans," meaning "nut of Jove;" *cinerea* means ash-colored; and "butternut" refers to the kernel, very rich in oil and of a butter-like flavor.

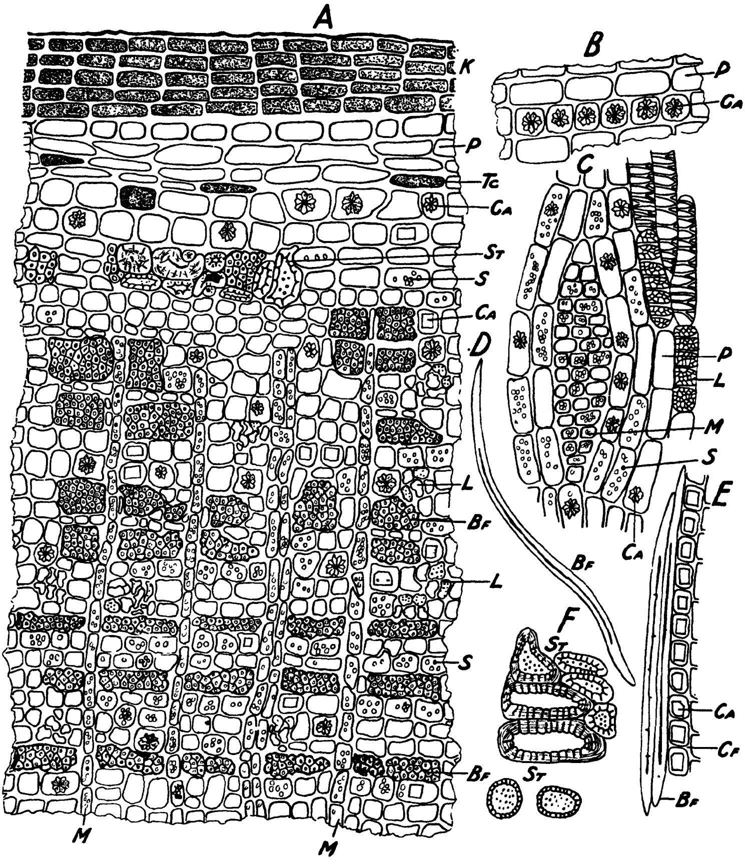


FIG. 96.—Juglans. *A*, transverse section showing cork (*K*); parenchyma cells (*P*); parenchyma cells filled with tannin (*Tc*); rosette aggregates and monoclinic prisms of calcium oxalate (*Ca*); stone cells (*St*); sieve (*L*); bast fibers (*Bf*); starch grains (*S*); medullary rays (*M*). *B*, fragment showing parenchyma cells (*P*), and rosette aggregates of calcium oxalate (*Ca*). C, tangential section showing medullary rays (*M*), sieve (*L*). *D*, bast fiber in longitudinal view. *E*, fragment in longitudinal view showing 4-sided calcium oxalate crystals (*Ca*) in cells forming a crystal fiber (*Cf*) and adjoining 2 bast fibers. *F*, characteristic stone cells (*St*). (Drawing by Hogstad.)

The bark occurs in quills or flattened, somewhat channeled pieces, of variable length and from 2 to 10 mm. in thickness; both the outer and inner surfaces are dark, the outer being somewhat scaly; fracture short, fibrous, the surface being somewhat checkered; odor distinct; taste bitter, astringent and acrid.

For the structure, see Figure 96.

The powdered drug is dark brown and exhibits calcium oxalate in rosette aggregates from 15 to 55 microns in diameter or in monoclinic prisms, from 10 to 50 microns in length, occurring in parenchyma or in crystal fibers; bast fibers, 30 microns wide and very long; stone cells, from 35 to 125 microns in length; oily drops and purplish brown tannin masses in parenchyma; starch grains mostly single, or 2- to 4-compound, the individual grains from 3 to 15 microns in diameter, occasionally with a central cleft.

Butternut bark contains about 7 per cent of a yellow, crystalline, acrid principle which is colored purple with alkalis; 2 to 2.5 per cent of a crystalline resin; volatile oil; tannin; sugar and a fixed oil. The total ash is from 4.65 to 7.05 per cent; acid-insoluble ash, from 0.1 to 0.4 per cent.

The bark is used as a mild cathartic. Average dose, 4 gm.

The root bark of *Juglans nigra* (black walnut) resembles butternut bark; but the crystal fibers with prismatic crystals are much more numerous.

BETULACEÆ, OR BIRCH FAMILY

This is a group of six genera of monœcious trees or shrubs. They are common to both hemispheres. The two genera of greatest importance are *Betula*, or birch, and *Corylus*, or hazelnut. The birches are extremely hardy and some grow within the Arctic Circle. They find a great many uses.

Oil of Sweet Birch (U. S. P. 1894 to 1916) is a volatile oil, obtained by distillation with steam of the twigs and bark of *Betula lenta*, the sweet or black birch, a tree growing in the eastern and north central portions of the United States. The oil does not pre-exist in the bark but is formed from the glucoside gaultherin, which very readily hydrolyzes in water to form methyl salicylate. This oil is one of the officially recognized forms of **methyl salicylate** (U. S. P. 1894 to date) (see page 481).

Birch Bark, the bark of the European white birch, *Betula alba*, is used to some extent in medicine as an astringent.

Rectified Birch Tar Oil, or Oleum Rusci (N. F. 1916 to date) is the pyroligneous oil obtained by the dry distillation of the bark and wood of *Betula pendula* Roth and related species of Betula, and rectified by steam distillation. The principal commercial sources are Russia, Poland and Finland.

PROPERTIES.—The oil is a limpid, dark brown liquid with a penetrating empyreumatic odor resembling that of Russia leather. It has a specific gravity between 0.886 and 0.950 and yields clear solutions with most solvents except methyl alcohol and water.

CONSTITUENTS.—Creosote, cresol, guaiacol, and a trace of phenol.

USES.—Rectified oil of birch tar is used externally in lotions or ointments as a counter-irritant, a parasiticide and an antiseptic in various skin diseases.

FAGACEÆ, OR BEECH FAMILY

This is a family of monœcious trees or shrubs which are of a very wide geographic distribution. The three general representatives are the beech (*Fagus*), the oak (*Quercus*), and the chestnut (*Castanea*).

THE BEECH (FAGUS)

The beeches are among the most beautiful forest trees. The wood is not affected when immersed in water, hence it is largely used in the construction of dams, water-mills, etc.

Beech Nuts have a delicate flavor as human food and are used largely for fattening swine in the fall of the year.

Beechwood Tar or Wood Tar is usually obtained from the destructive distillation of the wood of the European Red Beech (*Fagus sylvatica*) or the Southern Beech (*F. americana*). The distillation, carried out in heated iron retorts, yields three layers of distillate; a light and a heavy layer with an intervening aqueous stratum. The aqueous layer, known as pyroligneous acid, contains about 6 per cent of acetic acid and 1 per cent or more of methyl alcohol. The heavy layer is wood tar.

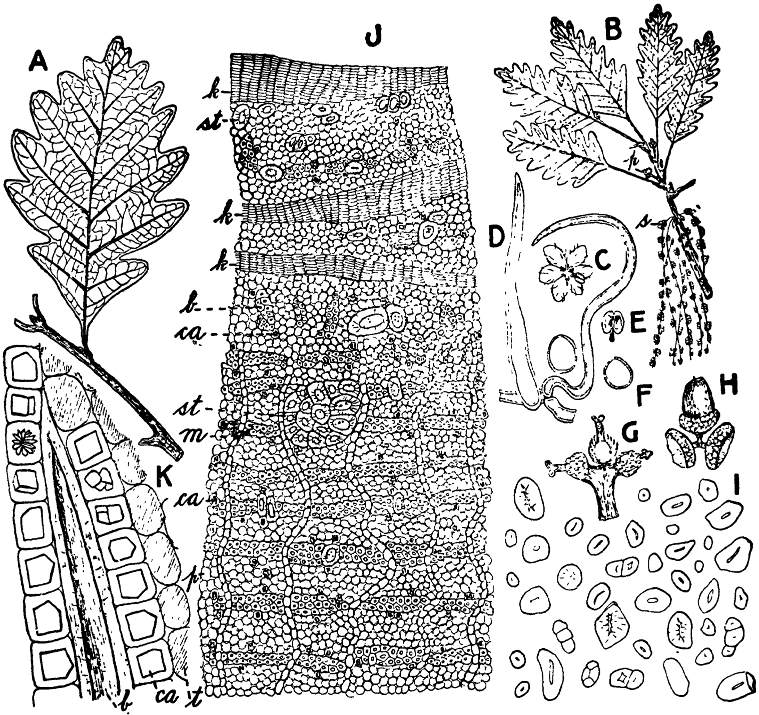


Fig. 97.—White oak (*Quercus alba*): *A*, characteristic, lobed leaf; *B*, young branch showing pistillate (*p*) and staminate (*s*) flowers; *C*, hairy bracts of a staminate flower; *D*, group of hairs from bract; *E*, stamen; *F*, pollen grains; *G*, cluster of pistillate flowers; *H*, acorn with cupule; *I*, starch grains from acorn, which vary from 10 to 25 microns long; *J*, transverse section of bark showing cork (*k*), stone cells (*st*), bast fibers (*b*), crystal fibers (*ca*), medullary rays (*m*), parenchyma (*p*); *K*, longitudinal section of bark showing end of bast fiber (*b*), crystal fibers (*ca*) and parenchyma cells (*t*) containing tannin.

Methanol, Methyl Alcohol or Wood Alcohol (in reagents, U. S. P. 1894 to date, and N. F. 1926 to date) is obtained from the aqueous layer of the distillate from the destructive distillation of wood or synthetically from carbon monoxide and hydrogen. It is used very extensively as a solvent and for other industrial purposes.

Creosote, Wood Creosote or Beechwood Creosote (U. S. P. 1842 to 1942; N. F. 1942 to date) is a mixture of phenols obtained from wood tar. The wood tar, upon distillation, yields a distillate with a heavy layer, which is again distilled, after treatment with sodium carbonate, only that portion of the distillate heavier than water being collected. This portion is purified with potassium hydroxide solution, sulfuric acid and redistillation until the potassium creosote solution does not turn brown upon being heated in air. The distillate boiling between 200° and 220° C. is retained.

Description and Properties.—Creosote is an almost colorless, or yellowish, highly refractive, oily liquid having a penetrating, smoky odor and a burning caustic taste. It is slightly soluble in water and is miscible with alcohol, there and fixed or volatile oils. Creosote should be free from phenol, coal-tar creosote, and hydrocarbons.

Constituents.—Creosote is a mixture of phenol compounds among which are guaiacol and cresol.

Uses and Dose.—Creosote is a stimulating expectorant. Average dose, 0.25 cc.

Creosote Carbonate (U. S. P. 1916 to 1942; N. F. 1942 to date) is a mixture of the carbonates of the various constituents of creosote. It is used as an expectorant pulmonary antiseptic and is preferable to creosote because it is more easily borne by the stomach and the kidneys. Average dose, 1 gm.

Guaiacol (U. S. P. 1905 to 1942; N. F. 1942 to date) is methylcatechol, first isolated from guaiac resin in 1826; now prepared by the fractional distillation of beechwood creosote and subsequent purification.

Guaiacol Carbonate (U. S. P. 1916 to 1936; N. F. 1936 to 1946) is a white, odorless, almost tasteless, crystalline powder, used mostly in veterinary practice as an intestinal antiseptic.

THE OAK (QUERCUS)

The oaks are among the most historic of our trees, and are noted for their strength, durability and longevity. Most species do not attain maturity before fifty or one hundred years, and some have attained an age of between five hundred and one thousand years. They furnish the most important woods of the world, the bark is used in tanning and dyeing and some species are used in medicine.

Acorns are largely used as a food for swine.

Cork of commerce is the inner bark of *Quercus suber* or *Quercus occidentailis*, indigenous to southwestern Europe, exported principally from Spain.

White Oak Bark (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the inner bark of *Quercus alba* Linné, a tree indigenous to the eastern and central United States and Canada. The bark from trees ten to twenty-five years old is collected in the spring, deprived of the periderm and dried.

The bark is in flat, irregular pieces, 2 to 10 mm. thick, yellowish brown, coarsely striate and with a coarse fibrous fracture. The taste is strongly astringent. For the structure, see Figure 97. The powder contains numerous long, thick-walled, strongly lignified bast fibers; crystal fibers; rosette aggregates and monoclinic prisms of calcium oxalate from 10 to 50 microns in length; a few stone cells; and parenchyma with yellowish brown tannin masses.

The drug contains tannin, about 10 per cent; the ash yield is up to 6 per cent, the acid-insoluble ash about 0.3 per cent.

White oak bark is used as an astringent and tonic. Average dose, 1 gm.

Black Oak Bark or Quercitron Bark (U. S. P. 1820 to 1873) is the inner bark of *Quercus velutina* Lamarck. It contains the glucoside quercitrin, which yields the yellow coloring matter quercetin (see page 311).

Oxalic Acid (U. S. P. 1873 to 1882; as reagent, U. S. P. 1894 to date; N. F. 1936 to date) is present in many plants, usually occurring as the potassium or calcium salt and was first isolated in 1769. It was made by the fusion of woody or cellulose matter such as sawdust with sodium hydroxide, or by oxidation with nitric acid. It has but little use in medicine but extensive use as a reagent and industrially.

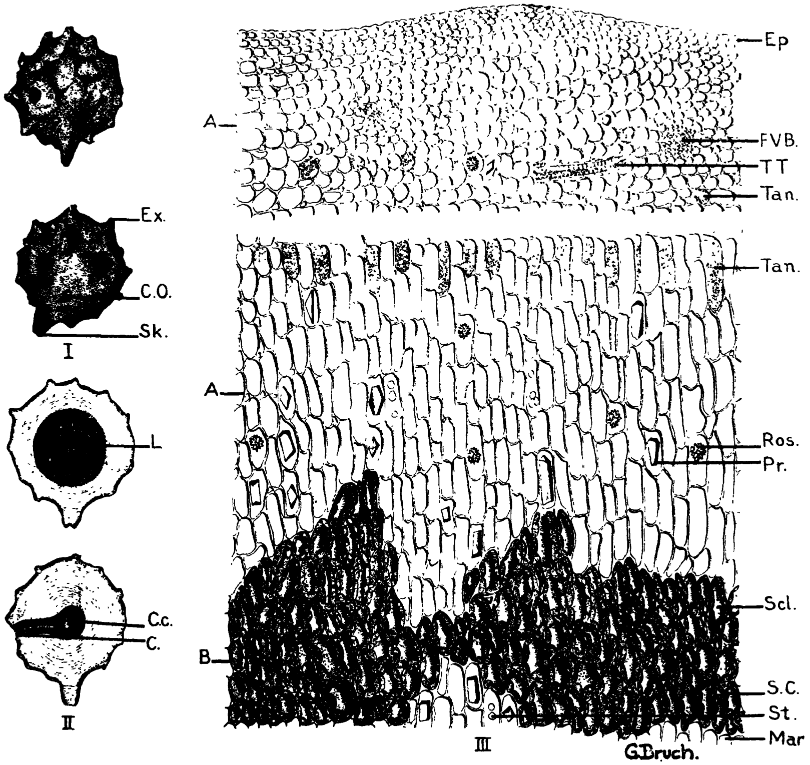


FIG. 98.—Nutgall. *I*, whole galls, somewhat spheroidal, 0.8 to 2.5 cm. in diameter; externally dark olive-green to grayish green, more or less tuberculate (*Ex*) above; the basal portion contracted into a short stalk (*Sk*) and nearly smooth; sometimes with a perforation (*CO*) on one side; dense, usually sinking in water; fracture short, horny. *II*, median longitudinal sectional views: internally grayish yellow to dark brown, with a central zone of starch-bearing cells and an outer, porous, lustrous zone of tannin-bearing cells, the two zones separated by layer of isodiametric stone cells or parenchyma cells with thick cellulose walls; frequently the central zone has formed into a cavity (*Cc*) containing a minute dead larva (*L*), or a radial canal (*C*) to the exterior is present and the cavity is empty; odor slight; taste strongly astringent. *III*, transverse section (in part), more highly magnified; *Ep*, epidermal cells; *FVB*, small fibrovascular bundles; *TT*, tracheal tubes; *Tan*, tannin cells; *Ros*, rosettes of calcium oxalate; *Pr*, prisms of calcium oxalate; *Scl*, stone cells; *St*, starch; *Mar*, margin of cavity. (Drawings by Gerston Bruch.)

Nutgall (U. S. P. 1820 to 1942; N. F. 1947 to date) is the excrescence obtained from the young twigs of *Quercus infectoria* Olivier and other allied species of *Quercus*. The galls are obtained principally from Aleppo, in Asiatic Turkey.

The excrescence (gall) is due to the puncture of a hymenopterous insect, *Cynips tinctoria*, and the presence of the deposited ovum; there are three stages in the development of the gall corresponding to the development of the insect:

1. When the larva begins to develop and the gall to enlarge, the cells of the outer and central zones contain numerous small starch grains.
2. When the chrysalis stage is reached, the starch near the middle of the gall is replaced in part by gallic acid, but the peripheral and central cells contain masses of tannic acid.
3. As the winged insect is developed nearly all of the cells contain masses of tannic acid with a slight amount of adhering gallic acid.
4. After the insect has emerged from the gall, leaving a hole to the central cavity, the tannic acid, due to the presence of moisture and air, may be oxidized in part into an insoluble product, and the gall becomes more porous, constituting the so-called **White Gall** of commerce.

The technical and medicinal use of galls was known to the ancient Greeks (450 B.C.). Ever since the Crusades, great quantities of them have been exported from Asia Minor.

DESCRIPTION, HISTOLOGY AND POWDER.—See Figure 98 and the National Formulary.

CONSTITUENTS.—The principal constituent is tannic acid, which is found to the extent of 50 to 70 per cent; the drug also contains gallic acid, 2 to 4 per cent; ellagic acid; starch and resin. Total ash 1.4 to 2.45 per cent; acid-insoluble ash about 0.1 per cent.

STANDARDS AND TESTS.—An aqueous mixture of powdered nutgall (1 in 10,000) gives a dark blue precipitate with 5 per cent ferric sulfate solution; a dark brown precipitate with 1 per cent ferric acetate solution; an orange-brown color and a slight precipitate with saturated potassium dichromate plus a trace of acetic acid; and a yellowish brown color and a slight precipitate with 1 per cent sodium carbonate solution.

USES AND DOSE.—Nutgall is the source of tannic acid and is used in the tanning and dyeing industry and in the manufacture of ink. Medicinally it is used as an astringent. Average dose, 0.5 gm.

ALLIED PRODUCTS.—**Japanese and Chinese Galls** are formed on *Rhus japonica* and *R. semialata* (Fam. *Anacardiaceæ*) respectively, due to the stings of certain plant lice (*Aphis*). These galls are very rich in tannin, and, as they contain less coloring matter than the oak galls, are used in the manufacture of gallic acid. They are irregular in shape, but somewhat ovoid, up to 5 cm. in diameter, more or less tuberculate, grayish brown, very hairy, buoyant and brittle. The wall is about 1 mm. thick, and the cavity contains the remains of numerous insects in the form of a grayish powder.

American nutgalls are formed on *Quercus coccinea* and *Q. imbricaria* by *Cynips aciculata*. When fresh they are globular, 1.5 to 3 cm. in diameter, and of a yellowish, somewhat mottled color. On drying they become yellowish to dark brown and much shriveled externally. **Texas nutgalls** are formed on the live oak (*Quercus virens*) and yield 40 per cent of tannic acid. **California oak galls** are excrescences on *Quercus lobata* and are about 5 cm. in diameter and said to contain considerable tannic acid.

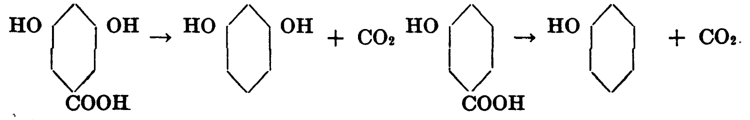
TANNINS

Tannins comprise a large group of substances which are widely distributed in plants; in fact practically every group of plants contains species which bear tannin to some extent. In plants that contain large amounts of tannin it is usually localized in specific plant parts. Being probably an end product of metabolism it is often found in dead tissue such as in the outer bark, in heartwood, in galls, etc. Tannins are also found in immature fruits but disappear upon the ripening of the fruit. It has been suggested by some that the fruit employs the energy supplied by the oxidation of these tannins in its metabolic processes, and by others that the tannins are the source of the fruit acids. One theory states that the tannins are "plant antiseptics" and as such prevent damage by fungi and insects. While these theories are somewhat speculative it appears to be apparent that, regardless of their purpose in plants, tannins are the end products of metabolism.

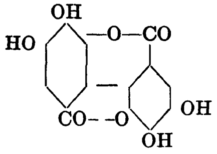
Tannins are non-crystalline substances which form colloidal solutions with water, these solutions possessing an acid reaction and a sharp astringent taste; they precipitate gelatin from solutions; they form dark blue or greenish black soluble compounds with ferric salts; they are precipitated by salts of copper, lead and tin or by strong aqueous potassium dichromate (or 1 per cent chromic acid); they precipitate alkaloids from solution; they produce a deep red color with potassium ferricyanide and ammonia and in alkaline solutions many of their derivatives readily absorb oxygen.

This property of precipitating proteins is the basis of the employment of tannins as astringents. In the treatment of burns, for example, the proteins of the exposed tissues are precipitated forming a mildly antiseptic, protective coat under which the regeneration of new tissue may take place. This property is also utilized in the tanning of hides to produce leather. The tannin is responsible not only for the pliancy and toughness of the leather, but is also antiseptic, thus acting as a preservative. Various types of tannins produce various types of leathers, thus the ellagic acid type produces a "bloom" while the phlobaphene type produces the "tanner's red." The deeply colored compounds obtained with iron salts have been utilized in the manufacture of ink, and because of their precipitation reactions, solutions of tannin are utilized in the laboratory as reagents for gelatin, proteins, alkaloids, etc.

Chemically tannins are complex substances. They usually occur as mixtures the separation of which is very difficult. Thus any chemical means of proving their constitution is almost hopeless. The tannin of greatest interest is gallotannin from nutgall. Fisher and Freudenberg believe gallotannin to be pentadigalloyl glucose, a condensation product of 1 molecule of glucose with 5 of digallic acid. On the other hand the work of Mitchell and Schmidt indicates the absence of glucose. Some workers believe that glucose may be present in gallotannin as an impurity, while others, as stated above, that it is an integral part of the molecule. While some tannins may appear to be glycosidic in nature the majority probably are not. When hydrolyzed or otherwise degraded they decompose into relatively simple polyhydric phenols among which are gallic acid, which decomposes further into pyrogallol, protocatechuic acid, which decomposes into catechol, ellagic acid, etc. The phenolic groups of the tannins are responsible for their astringent and antiseptic action as well as their coloration with iron salts.



Gallic acid　Pyrogallol　Protocatechuic acid　Catechol



Ellagic acid

The classification of tannins is usually based upon the colors obtained with iron salts. It has definitely been demonstrated that in the presence of catechol with its two adjacent phenolic groups, a green color is obtained with ferric iron and in the presence of pyrogallol with three adjacent phenolic groups a blue color. In practice, however, where tannins of both types may be present in the same plant extract, the one present in larger amount will mask the one present in lesser amount. Then too, tannins of the ellagic acid type, which contain pyrogallol nuclei will produce a green coloration because of the two free phenolic groups. The usual classification of tannins is as follows:

1. **Phlobatannins** (also known as catechol or pyrocatechol tannins), which yield catechol upon heating; when boiled with HCl they yield red insoluble phlobaphenes; with $FeCl_3$ they form a green color; and with bromine water a precipitate. (Such tannins are found in kino, gambir and catechu.)
2. **Pyrogallotannins,** which yield pyrogallol upon heating; when boiled with HCl they yield gallic or ellagic acids; with $FeCl_3$ they form a blue color; and with bromine they yield no precipitate. (Examples: Gallotannin found in nutgall; ellagitannin found in oak bark and pomegranate bark.)
3. **Pseudotannins,** which do not tan leather but yield colors with iron salts. (Gallic Acid is a pseudotannin.)

Tannic Acid, Gallotannic Acid, or Tannin (U. S. P. 1842 to date; as reagent, U. S. P. 1882 to date; N. F. 1936 to date) is a tannin usually obtained from nutgall. The powdered galls are extracted with a mixture of ether, alcohol and water; the liquid separates into two layers, the aqueous layer containing gallitannin and the ethereal layer the free gallic acid present in the gall. After separation the solution of gallitannin is evaporated, the tannin being purified in various ways. Acetone and other solvents are sometimes used and it is said that a considerable amount of commercial tannin comes from Chinese and Japanese galls.

DESCRIPTION AND TESTS.—Amorphous powder, glistening scales or spongy masses, light brown to yellowish white; odor faint; taste strongly astringent. Tannic acid is soluble in water, alcohol and acetone, and insoluble in ether, chloroform and benzin. An aqueous solution of tannic acid is colored bluish black with ferric chloride T.S., and precipitates alkaloids, albumin and gelatin from solution. Tannic acid loses not more than 12 per cent of its weight upon drying at 100° C. and yields not more than 0.5 per cent of ash. It should be free from gum, dextrin, and resinous substances.

USES AND DOSE.—Tannic acid is used in the treatment of burns, and as an astringent. Average dose, 1 gm.

Acetyltannic Acid or Diacetyl Tannic Acid (U. S. P. 1926 to 1942) is a product obtained by the acetylization of tannic acid. Average dose, 0.6 gm.

Albumin Tannate (U. S. P. 1926 to 1942) is a compound of albumin (usually egg albumin) and tannic acid. Average dose, 2 gm.

Gallic Acid (U. S. P. 1851 to 1926; N. F. 1936 to 1947; as reagent, U. S. P. 1926 to date) is 3:4:5 trihydroxybenzoic acid, crystallizing with one molecule of water. It occurs in nutgall or may be prepared from tannic acid by hydrolysis with dilute acids (see page 214).

Gallic acid occurs as white or fawn-colored silky needles having an astringent slightly acidulous taste; soluble in water and in alcohol but insoluble in chloroform. It loses not more than 12 per cent of its weight upon drying at 100° C.; it yields not more than 0.1 per cent of ash; it neither colors nor precipitates pure ferrous salts and should be free from tannic acid.

Gallic acid is a mild astringent. Average dose, 1 gm.

Pyrogallol, or Pyrogallic Acid (U. S. P. 1894 to 1942; N. F. 1942 to date; as reagent, U. S. P. 1916 to date) is 1:2:3, trihydroxybenzene, and is obtained by heating gallic acid (see page 214).

Description and Tests.—White leaflets or fine needles, soluble in water, alcohol, and ether. Melting-point, 130° to 133° C. Pyrogallol in solution is rapidly oxidized by the air, especially in the presence of alkalis. Pyrogallol in a 1 in 10 solution reduces salts of silver, gold and mercury.

Uses.—Pyrogallol is used externally as an irritant and antiseptic in skin affections.

THE CHESTNUT (CASTANEA)

The chestnuts constitute very useful and ornamental trees. There are three well-known species, namely: *Castanea sativa* or European Chestnut; *C. dentata* or American Chestnut; and *C. crenata* or Japanese Chestnut.

The **nuts** are an important article of food in many nations, used toasted or boiled for humans and raw by swine and other animals. The large Spanish nuts are extensively exported.

The **timber** is much like that of oak, but finer grained. It is used as a finishing lumber. **Chestnut Extract**, a tanning material, is prepared from the wood and bark and contains 26 to 30 per cent of tannin, and is used especially for sole leather.

An **extract** of the leaves is used as a mild astringent in medicine.

A fungus disease attacks the bark of the chestnut in Asia, but the Japanese trees are sufficiently resistant as not to be killed. This fungus was introduced into the United States and it has nearly destroyed the American chestnut forests. Resistant strains have been developed and are now being planted in the chestnut area of the United States, from Maine to Michigan and south to North Carolina and Mississippi.

Chestnut Leaves (U. S. P. 1873 to 1905; N. F. 1916 to 1947) consist of the dried leaves of *Castanea dentata* (Marshall) Borkhausen. The leaves are gathered at the time of flowering of the tree or shortly afterward and are carefully dried.

Description, Structure and Powder.—See Figure 99 and the National Formulatory, 7th edition.

Chestnut leaves contain 9 per cent of tannic acid, colored green with ferric salts and not precipitated with a solution of tartar emetic; also mucilage which is insoluble in alcohol. It is used as a tonic and an astringent. Average dose, 4 gm.

Chinquapin Bark (U. S. P. 1820 to 1851) is the dried bark of *Castanea pumila* Michaux. This bark, like that of the chestnut, contains tannin and has been used as an astringent. The seeds are smaller than chestnuts but contain about 45 per cent of starch and 2.5 per cent of protein.

ULMACEÆ, OR ELM FAMILY

This family consists mostly of shrubs and trees growing in the tropics and in temperate regions. Many of the plants of this family have distinct mucilage cells. In *Ulmus* they are very prominent in the form of short, broad cylindrical cells, regularly arranged in the squares formed by the tangential rows of bast crossing the medullary rays, giving the transverse section a checkered appearance.

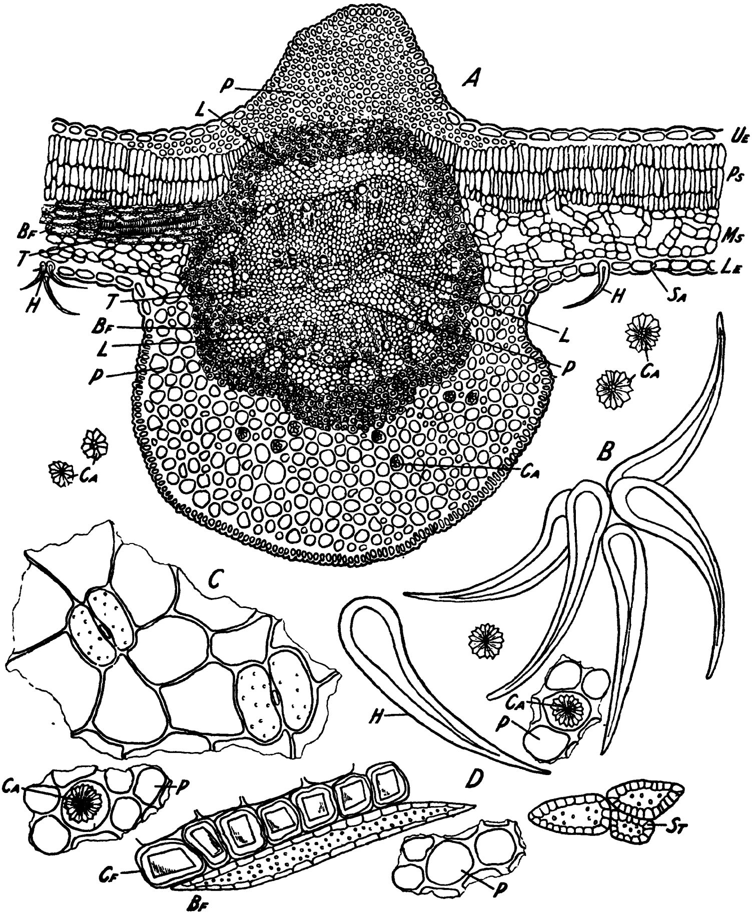


Fig. 99.—Castanea. *A*, transverse section of leaf through the midrib showing upper epidermis (*Ue*); palisade layers (*Ps*); loose mesophyll (*Ms*); bast fibers (*Bf*); sieve (*L*); tracheæ (*T*); parenchyma (*P*); non-glandular hairs (*H*); rosette aggregates of calcium oxalate (*Ca*); stoma (*Sa*); lower epidermis (*Le*). *B*, stellate hair. *C*, fragment of leaf showing 2 stomata. *D*, fragments of powdered drug showing crystal fiber (*Cf*); bast fiber (*Bf*); stone cells (*St*); parenchyma (*P*) containing calcium oxalate (*Ca*); non-glandular hair (*H*). (Drawing by Haase.)

ELM

Elm; Elm Bark, or Slippery Elm (U. S. P. 1820 to 1936; N. F. 1936 to date) is the dried inner bark of *Ulmus fulva* Michaux, a tree indigenous to the eastern and central United States and Canada. The generic name *Ulmus* is the classic name of the elm; *fulva* means "yellow" or "tawny," and is applied because the bark is of this color. The bark is collected in spring, deprived of the periderm and dried, the commercial article coming chiefly from Michigan.

Description.—In flat, oblong pieces 1 to 4 mm. thick; outer surface weak yellowish orange, longitudinally wrinkled and furrowed and with occasional dark brown patches of periderm; inner surface usually finely striated longitudinally; fracture fibrous, porous from large mucilage cells.

Structure.—See Figure 100.

Powder.—Weak yellowish orange in color; odor distinctive, suggesting fenugreek; taste mucilaginous. Bast fibers are numerous, very long, up to 25 microns in diameter, thick-walled, unlignified, or but slightly so; calcium oxalate in monoclinic prisms, mostly in crystal fibers, the individual crystals from 10 to 35 microns in length; fragments of large mucilage cells with adhering starch grains; the latter mostly spheroidal or polygonal, usually 3 to 15 microns in diameter, with a maximum length of 25 microns.

Constituents.—The principal constituent of elm bark is mucilage; it also contains starch and calcium oxalate. Total ash from 7.45 to 9.92 per cent; acid-insoluble ash up to 0.62 per cent.

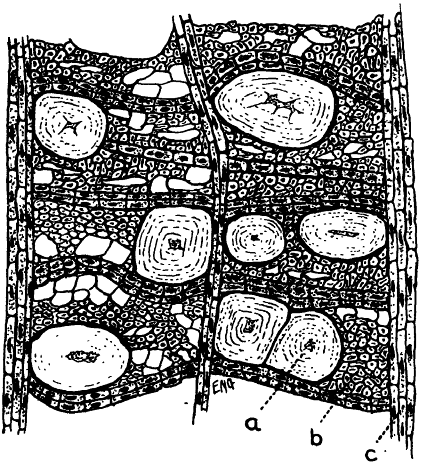


Fig. 100.—Elm Bark: *b*, bundles of small, thick-walled but slightly lignified bast fibers associated with large mucilage cells (*a*) up to 400 microns in diameter, small strands of sieve, and parenchyma cells containing starch or prisms of calcium oxalate, the crystal cells frequently elongated and the crystals super-imposed so as to form short non-lignified crystal fibers; *c*, medullary rays 2 to 6 cells wide, bearing starch, and forming in transverse sectional view distinct squares with the tangential plates of leptome. (Drawing by E. N. Gathercoal.)

Standards.—Good elm bark yields a rather thick mucilage when 1 part of the ground bark is digested in 40 parts of cold water for one hour.

Uses and Dose.—Ulmus is a demulcent and an emollient. Average dose, *ad libitum.*

Adulterants and Allied Products.—Ground elm bark has been reported to be adulterated with wheat starch or wheat middlings. It may also be adulterated with a bark from which the mucilage has been extracted or with barks poor in mucilage. *Ulmus campestris*, or European Elm, yields a bark which is dark brown, and contains, besides mucilage, a bitter principle and tannin.

MORACEÆ, OR MULBERRY FAMILY

These are herbs, shrubs or trees, distinguished for the most part by having laticiferous cells, which occur in both the axis and leaves of the mature plant. The laticiferous tubes in the pith often extend through the medullary rays, uniting with those in the cortex. In the leaves of some species of *Ficus,* the laticiferous tubes are found associated with vascular bundles only, while in other species, as the common rubber plant in cultivation (*Ficus elastica*), the tubes send out branches which traverse the mesophyll tissue. *Ficus elastica* yields **Assam rubber,** while *Castilla elastica* yields **Central American rubber.** Cystoliths and long bast fibers commonly occur in the family.

Cannabis, Indian Hemp, American Hemp (U. S. P. 1873 to 1942) consists of the dried flowering tops of the pistillate plants of *Cannabis sativa* Linné; an extract of Indian hemp was recognized in the U. S. P. of 1862, though the drug itself was not recognized.

The plant is an annual herb indigenous to central and western Asia, and is cultivated in India and other tropical and temperate regions for the fiber and seed. *Cannabis* is the ancient Greek name for hemp.

Cannabis was used in China and India, spreading slowly through Persia to the Arabs, and it probably was introduced into European and American materia medica about the time of Napoleon.

The amount of resin found in the pistillate flowering tops of *Cannabis sativa* markedly decreases as the plants are grown in the more temperate climates. Thus Indian cannabis yields 20 per cent or more of resin; Mexican cannabis 15 per cent or less; Kentucky hemp 8 per cent or less; Wisconsin hemp 6 per cent or less. The active principles are found in the resin in about the same, or even smaller, ratio as that indicated above. The hemp leaves contain a small amount of the resin.

Indian cannabis is prepared rather carefully from the pistillate flowerheads only, with relatively few leaves, but Mexican and American cannabis consist of the whole upper portion of the stalk of the pistillate plant. Indian cannabis may have an activity about ten times as great as that of a poor quality of American cannabis.

The U. S. Pharmacopœia recognized Cannabis Americana in a separate monograph in the 1870 and the 1880 revisions, then the monograph was deleted because of poor quality drug. During World War I (1914 to 1918) the importation of Indian cannabis ceased, and as a war measure, American cannabis was permitted in the cannabis monograph in the U. S. P. of 1916. It remained in the monograph until the drug was deleted in 1942.

The pleasurable sensations induced in man by the controlled use of cannabis are obtained from inhaling the smoke of burning cannabis, more promptly and with less drug, than by oral dosage. Some decades ago unscrupulous persons began the importation into the United States of rather crude **Mexican cannabis** (**Marihuana**) cigarettes for sale at high prices. As the demand for these cigarettes increased and the habit of smoking them spread even to school children, federal and state narcotic agents started a campaign to stamp out their sale. The importation of Indian cannabis was prohibited and even large areas of growing American hemp were destroyed. This campaign has been successful; however, the official substitution of a poor quality drug for the high quality Indian cannabis, along with the marihuana campaign, has cost the materia medica a valuable drug, for the medicinal use of cannabis in the United States has been discontinued.

For the description of the whole drug and characteristics of the powdered drug, see Figure 101 and the U. S. Pharmacopœia, 11th revision.

Indian cannabis contains 15 to 20 per cent of a resin, cannabin; cannabinol (cannabindon), a red, oily substance said to possess the intoxicating properties of the drug; a yellowish volatile oil; a volatile alkaloid, cannabinine; ash from 12.2 to 18 per cent, with about 2.75 per cent of acid-insoluble ash, the latter being made up largely of fragments of the silicified non-glandular hairs. The drug is said to lose its activity when in the powdered condition. It is a sedative, an analgesic and a narcotic. Average dose, 100 mg.

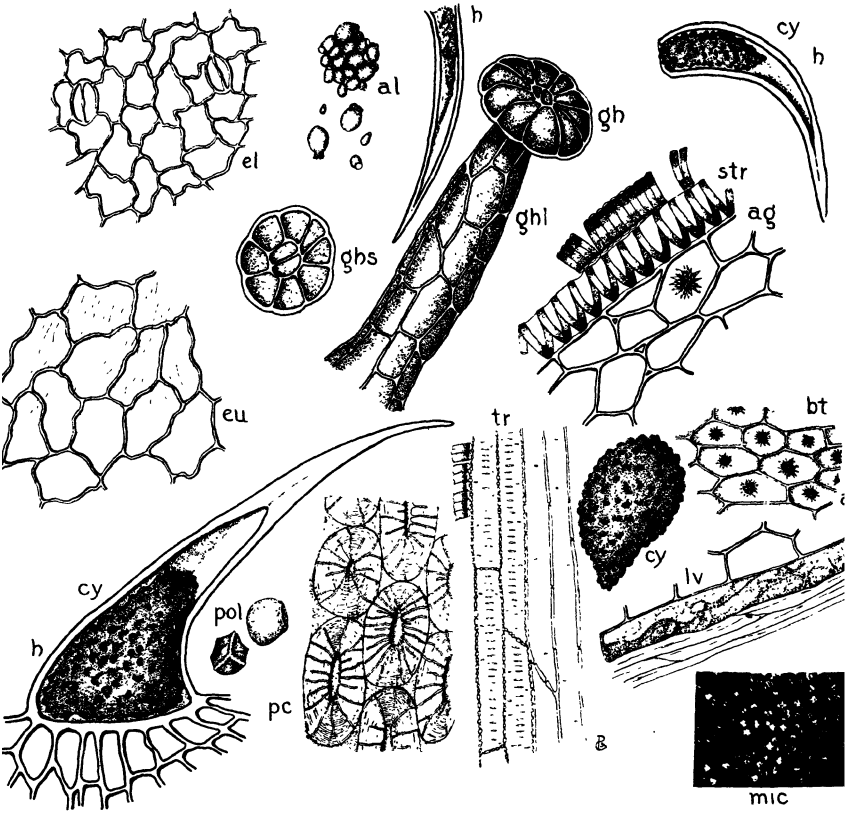


FIG. 101 —Powdered Cannabis Indica: *el*, epidermis from lower surface of leaves with sinuate vertical walls and numerous oval stomata, and *eu*, from upper surface, with straight walls and no stomata; *h*, non-glandular hairs—numerous, unicellular, rigid, curved, with a slender pointed apex and an enlarged base, usually containing a cystolith (*cy*) but frequently broken and the cystolith freed; glandular hairs of two kinds, one with a short 1-celled stalk (*ghs*) and the other with a long multicellular stalk (*ghl*), the head (*gh*) in both kinds being globular and consisting of 8 to 16 cells; *bt*, fragments of bracts and leaves showing yellowish brown laticiferous vessels (*lv*), numerous rosette aggregates (*ag*) of calcium oxalate, 5 to 30 microns in diameter, strands of spiral (*str*) or reticulate (*tr*) tracheæ, and phloem; (*pc*), fragments of fruits with palisade-like, non-lignified cells with yellowish brown, finely porous walls; tissues of embryo and endosperm with numerous oil globules and aleurone grains (*al*), the latter 5 to 10 microns in diameter and displaying crystalloids and globoids; *pol*, pollen grains; *mic*, photomicrograph of leaf fragment showing a rosette aggregate of calcium oxalate crystals in nearly every cell. (Drawings by Paul D. Carpenter.)

ALLIED PRODUCTS.—An **African Cannabis** has been imported which, while not of as good appearance as the East Indian drug, yielded 14.06 per cent of a resin having full therapeutic activity. A **Turkish cannabis** has been imported which yielded 9 per cent of resin, having the average therapeutic activity of the standard drug. Physiologically active cannabis also comes from Turkestan, Asia Minor, France, Italy, Spain and Mexico, and from the warmer and more arid regions in the United States.

Cannabis is cultivated to a considerable extent for its bast fibers, **hemp,** and fruits, **hempseed;** the latter contain about 20 per cent of a fixed oil which is used for culinary purposes and in the manufacture of paints and soap, the cake meal being used as cattle food.

Humulus or Hops (U. S. P. 1820 to 1926; N. F. 1926 to 1947) is the dried strobile of *Humulus lupulus* Linné bearing its glandular hairs. The plant is a perennial herbaceous climber, indigenous to Europe, Asia and North America, and extensively cultivated in England, Germany and various parts of the United States, South America and Australia, where it is also naturalized.

Hops are collected in September, when they are ripe, carefully dried by means of artificial heat, and packed into bales or bags. They are sometimes treated with sulfur dioxide to improve the color and to prevent change of the active principles.

The strobiles are ovoid-cylindrical, up to 3 cm. long and 2 cm. wide with a sharply undulate rachis and about 50 membranous bracts; color pale yellow green; odor strongly aromatic and characteristic; taste aromatic and bitter. The numerous, orange colored glandular trichomes at the base of the bracts are the important characteristic of the powder. The bracts and rachis of humulus contain tannin but the glandular hairs give the principal activity to the drug.

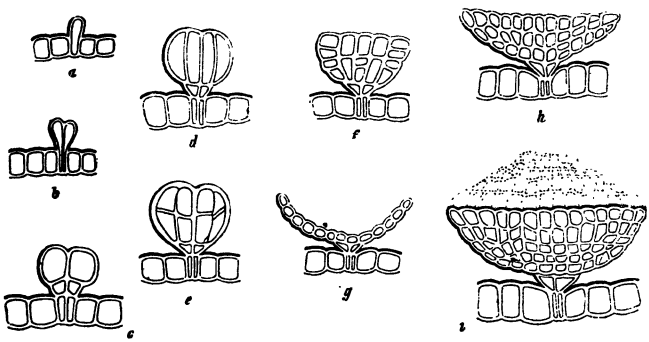


FIG. 102.—Lupulin: *a*—*h*, successive stages in the development of the glandular hairs on the bracts and floral envelopes of Humulus; *g*, longitudinal section through a mature hair as seen at *h*; *i*, glandular hair with the cuticle raised due to the accumulation and pressure of the oily secretion beneath it. (After Holzner.)

Humulus deteriorates upon aging and exposure to the atmosphere. The loss of the pale green color in the bracts; the development of a valerian-like odor and of a disagreeable, nauseating taste indicate badly deteriorated drug. It is a stomachic, a sedative and a tonic. Average dose, 2 gm.

Lupulin (U. S. P. 1831 to 1916; N. F. 1916 to 1947) consists of the glandular trichomes separated from the strobiles of *Humulus lupulus* Linné. Commercial Lupulin consists mostly of sweepings collected where hops are prepared for the market, the extraneous matter being removed by sifting and washing. The powder has been carefully dried and preserved.

Lupulin is a bright, yellowish orange, granular powder consisting of trichomes with a somewhat globular, multicellular head 100 to 300 microns in diameter, with a single layer of secreting cells arranged in the form of a shallow cup, from the inner surface of which the cuticle has been separated by the secreted oleoresin; odor aromatic, characteristic of hops; taste aromatic and bitter. In fresh lupulin the glandular hairs mostly contain light yellow oleoresin; but upon aging, this oleoresin becomes grayish brown and resinous, and the odor becomes valeric and disagreeable.

Lupulin contains a volatile oil consisting largely of a terpene called humulene, and also containing esters of valeric and other acids; a bitter principle humulol; resin and wax. Total ash, about 11 per cent with about 2.5 per cent of acid-insoluble ash in which can be seen, under the microscope, the remains of the silicified cell walls of the drug.

Lupulin yields not less than 60 per cent of non-volatile ether-soluble extract and not more than 10 per cent of acid-insoluble ash. It should not have a dark reddish brown color and a disagreeable, valerian-like odor.

USES AND DOSE.—Lupulin is a bitter tonic, a sedative and a hypnotic. Average dose, 0.5 gm.

Ficus or Fig (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the partially dried fruit of *Ficus carica,* a tree indigenous to Persia and cultivated in most subtropical and tropical countries. The fig contains 50 to 60 per cent of glucose and is eaten as a nutrient, demulcent and laxative.

Other species of *Ficus* also yield edible figs, as the mulberry fig tree, *F. sycomorus,* of Africa; *F. religiosa,* of India; *F. glomerata,* of Burma; the false banyan tree, *F. bengalensis,* of tropical Africa and India, and *F. rumphii* of Asia.

A peptonizing ferment is obtained from the milk-juice of *Ficus carica, F. sycomorus* and *F. exima,* of Brazil.

When figs are dried, roasted and ground, they form a coffee substitute known as **Fig Coffee,** which is also used sometimes as an adulterant of coffee. It is detected by the large, thin-walled and broad, non-glandular hairs of the outer epidermis; the broad latex tubes, 30 to 50 microns in width; and the small achenes. The latter somewhat resemble the achenes of strawberry fruits, but are distinguished by the reticulated thickening of the outer cell wall.

URTICACEÆ, OR NETTLE FAMILY

Urtica or Stinging Nettle is the flowering plant of *Urtica urens* and *Urtica dioica.* The plants are rather common in waste places of Europe and the United States, the former being known as the small nettle and the latter as the stinging or great nettle. *Urtica urens* is an annual herb, while *Urtica dioica* is a perennial herb. The leaves and flowering tops are gathered in the late summer. It was formerly stated that the stinging action was due to the presence of formic acid. In the light of later research this seems doubtful and the activity is now ascribed to a ferment. The plant contains a glucoside, a tannin, mucilage, a coloring principle and possibly also an alkaloid.

Urtica is a powerful diuretic. Average dose, 45 cc. of the decoction.

SANTALACEÆ, OR SANDALWOOD FAMILY

Most of the members of this family are shrubs or trees indigenous to the tropics. A few are found growing in the United States, as the Oil-nut or Buffalo-nut (*Pyrularia pubera*), the fleshy fruit of which is edible and the seeds of which contain an acrid fixed oil. Others are parasitic on the roots of other plants. There are 26 genera with about 250 species.

White Sandalwood (N. F. 1916 to 1947) is the heartwood of *Santalum album* Linné, a parasitic tree indigenous to India. It attains a height of 10 meters and produces a dense evergreen foliage. It is extensively cultivated in southeastern

Asia and the Sandalwood Islands of the Indian Archipelago, the present supply coming largely from southern India. The heartwood from twenty to forty-year old trees is cut into billets, the most select wood being retained in India for distillation of the oil, and the wood of the smaller stems or branches exported through Bombay to China, Europe and the United States.

Sandalwood contains 1.5 to 6 per cent of volatile oil. The wood is used in the manufacture of incense, and as a source of the volatile oil to which it owes its antiseptic and stimulant properties.

Sandalwood occurs in billets, pieces, or chips of varying shapes and sizes, heavy, hard, but splitting easily; color light yellowish brown with alternating lighter and darker concentric zones nearly equal in width. Odor characteristic, aromatic, persistent; taste peculiar, strongly aromatic.

It displays many very narrow medullary rays from one to four cells wide, the cells thick-walled and radially marked; tracheæ large, numerous, usually solitary, with bordered pores; wood fibers numerous, with pointed ends and porous walls, occasionally with a few starch grains up to 15 microns in diameter; wood parenchyma containing single crystals of calcium oxalate up to 30 microns in length; oil in globules adhering to the walls of the tracheæ and parenchyma cells, especially rich in the medullary ray cells.

Santal Oil, Sandalwood Oil (U. S. P. 1882 to 1942; N. F. 1942 to date) is the volatile oil distilled with steam from the dried heartwood of *Santalum album* Linné.

DESCRIPTION.—A pale yellow, somewhat viscid, oily liquid having the odor and taste of sandalwood. The oil contains about 95 per cent of a mixture of sesquiterpene alcohols known as santalol and consisting of α-santalol (B. P. 300° C.) and β-santalol (B. P. 170° C.) as well as small quantities of esters, ketones and other alcohols and aldehydes.

STANDARDS.—Santal Oil yields not less than 90 per cent of alcohols calculated as santalol ($C_{15}H_{24}O$). Some foreign pharmacopœias also require the oil to yield not less than 2 per cent of esters calculated as santalyl acetate.

USES AND DOSE.—Oil of Santal is a urinary antiseptic and stimulant and to some extent an expectorant in bronchitis. Average dose, 0.5 cc. It is also employed in the manufacture of perfumes.

ALLIED PRODUCTS.—**West Australian Sandalwood Oil** is obtained by the distillation of the wood of *Eucarya spicata* and is used in India and China as a substitute for the genuine oil. It contains sesquiterpene alcohols known as "fusanols," in a quantity less than 90 per cent, but the oil may be rectified to yield this percentage. **West Indian Sandalwood Oil** is obtained from *Amyris balsamifera* (Fam. *Rutaceæ*). **South Australian Sandalwood Oil** is derived from *Santalum preissianum* and has a cherry-red color, with an odor similar to that of roses. **East African Sandalwood Oil** is obtained from *Osyris tenuifolia* and has an odor resembling that of West Indian Sandalwood Oil. **Fiji Sandalwood Oil** is obtained from *Santalum yasi.*

ARISTOLOCHIACEÆ, OR BIRTHWORT FAMILY

These are herbs or twining woody plants with reniform or cordate, palmi-nerved leaves. There are about 200 species, mostly represented in tropical and subtropical countries, of which about 180 belong to the genus *Aristolochia.* The family is especially characterized by the presence of secretory cells containing a volatile oil. Tannin-containing cells are also present in certain of the *Aristolochiæ.* Cells with silicified walls are found in the upper epidermis of the leaf and the palisade tissue. A non-glandular hair, the terminal cell of which is curved like a hook, is rather characteristic in *Aristolochia* and other genera.

SERPENTARIA

Serpentaria (U. S. P. 1820 to 1942; N. F. 1942 to date) consists of the dried rhizome and roots of *Aristolochia serpentaria* Linné, known in commerce as **Virginia Snakeroot,** or of *Aristolochia reticulata* Nuttall (U. S. P. 1851 to 1942; N. F. 1942 to date), known in commerce as **Texas Snakeroot.**

Virginia snakeroot is found growing from New England to Florida and west to Michigan and Missouri. Texas or Red River Snakeroot is collected in the woods of Texas, Louisiana, Arkansas and Oklahoma. The generic name *Aristolochia* means "an aid in childbirth," although the drug probably does not possess any value for this purpose; *serpentaria* refers to the twining of the vine in a snake-like fashion; and *reticulata* to the network of veins in the leaves. The rhizome and roots are collected in autumn and dried.

Description and Structure.—See Figures 103 and 104 and the National Formulary.

Powder.—Pale brown to dusky yellow; odor camphoraceous or terebinthinate; taste bitter, aromatic; starch grains numerous, single and 2- to 4-compound, the individual grains more or less spheroidal or plano-convex, from 3 to 18 microns in diameter, and frequently with a central cleft; lignified elements numerous, consisting of tracheæ, wood fibers, medullary ray cells and pith cells; a few typical non-glandular hairs of the stem are occasionally present.

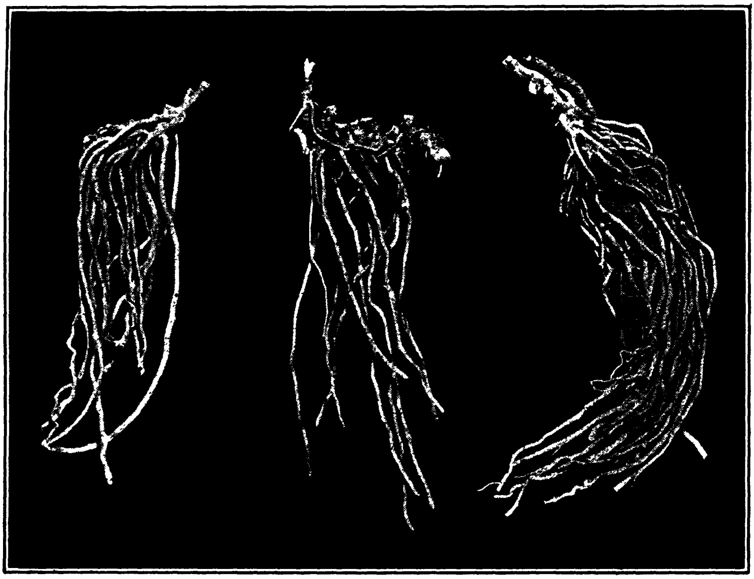


Fig. 103.—Serpentaria. The dried rhizome and roots, with a little overground stem projecting at the top of *Aristolochia serpentaria*, which constitutes the official drug. (Photo by Paul D. Carpenter.)

Constituents.—Volatile oil 0.5 to 2 per cent, the important constituent of which is borneol; a bitter poisonous principle, aristolochin, also known as serpentarin and an alkaloidal principle, aristolochine; several organic acids; starch; total ash about 5.75 per cent; acid-insoluble ash about 2.75 per cent in carefully cleaned drug.

Standards.—Serpentaria contains not more than 10 per cent of its overground stems and not more than 2 per cent of other foreign organic matter, and yields not more than 10 per cent of acid-insoluble ash.

Uses and Dose.—Serpentaria is an aromatic, bitter stimulant and a tonic. Average dose, 1 gm.

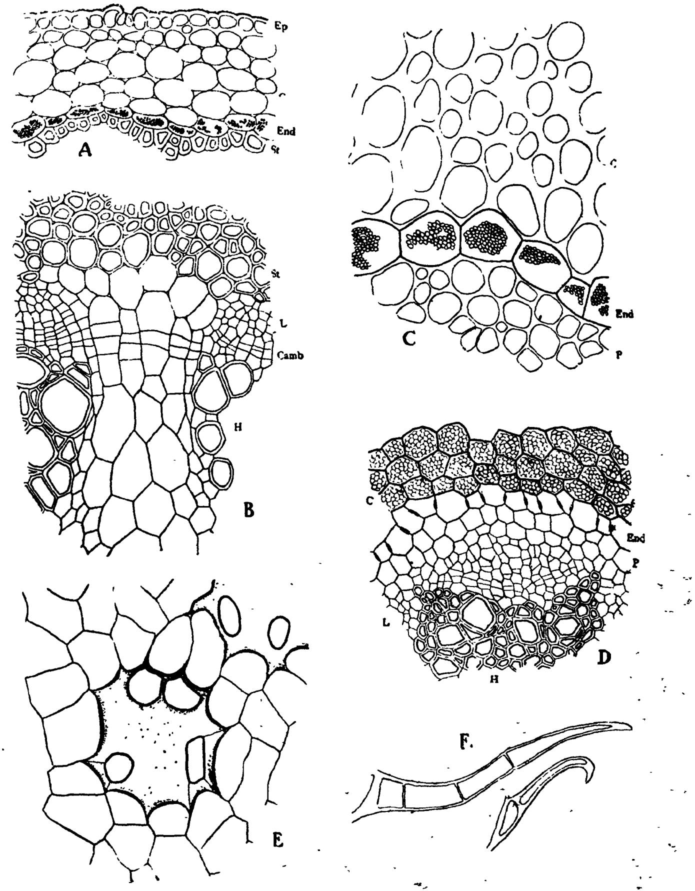


Fig. 104.—Serpentaria. *A* and *B*, transverse section of stem-internode: *Ep*, epidermis with a single stoma; *c*, cortex, the outer cells collenchymatous and with the parenchyma, containing chloroplasts and oil; *End*, endodermis of thin-walled starch-bearing cells; *St*, pericycle of several layers of thick-walled sclerenchymatous fibers; *L*, phloem; *H*, tracheæ of the vascular bundle. *C*, transverse section of a swollen node showing collenchyma (*c*) of which the entire cortex is made up; starch-bearing endodermis (*End*) and pericycle (*P*) which is very much reduced. *D*, transverse section of a secondary root showing starch-bearing parenchyma cells of cortex (*C*); endodermis (*End*) of thin-walled cells with distinct Casparyan spots and free from starch; pericambium (*P*); phloem (*L*); wood (*H*). *E*, epidermis with silicified cells from the upper or ventral surface of the lamina of the leaf which are the cause of the small perforations seen in the leaf blade when held toward the light. *F*, non-glandular hairs from the leaf, one of which is very prominently curved, forming a small hook. (After Holm.)

SUBSTITUTES.—The rhizome of Yellow Root (*Jeffersonia diphylla*, Fam. *Berberidaceæ*) is sometimes substituted for serpentaria, from which it is distinguished by its lack of odor and by having a bitter, acrid taste.

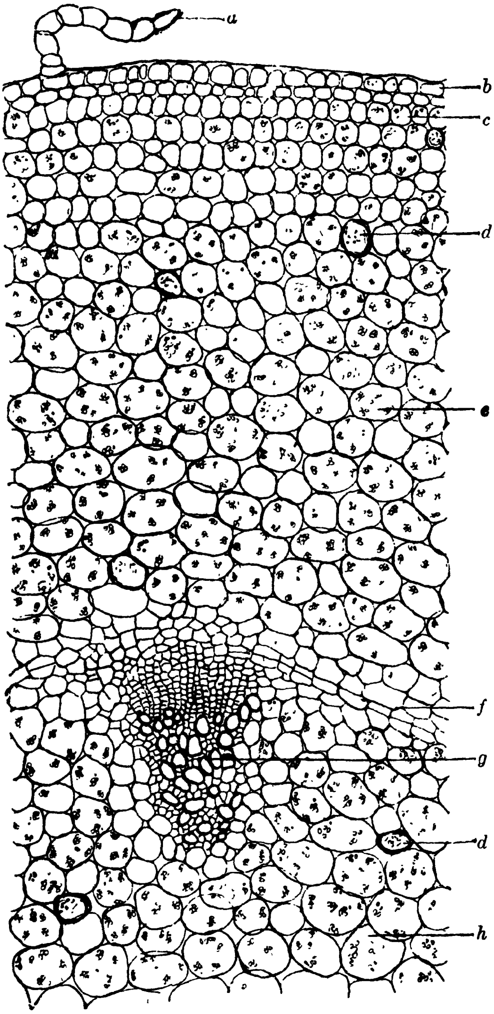


FIG. 105.—Asarum. Transverse section of the rhizome showing a uniseriate nonglandular hair (*a*); epidermal layer (*b*); several layers of collenchymatous cells (*c*); starch-bearing parenchyma of cortex (*e*); oil cells with suberized walls (*d*); endodermis (*f*); tracheæ (*g*) with spiral or scalariform thickenings of the wall and associated with small tracheids; starch-bearing parenchyma of pith (*h*). (After Bastin.)

Asarum, Wild Ginger, or Canada Snakeroot (U. S. P. 1820 to 1873; N. F. 1916 to 1947) is the dried rhizome and roots of *Asarum canadense* Linné. The plant is an acaulescent, perennial herb growing in rich woods of the northern and central United States and southern Canada.

The rhizome is gathered in the spring, usually deprived of the roots and carefully cleaned and then dried, most of the supplies coming from North Carolina, Virginia, Indiana and Michigan.

Asarum rhizome is horizontal, 2 to 4 mm. thick, occasionally branched, quadrangular, finely striate, more or less twisted; the nodes are enlarged, with irregular scars from petioles and remains of pedicels; the internodes have annular scars from scales; fracture short; externally from yellowish to reddish brown; internally whitish, starchy or resinous. Roots few, up to 7 cm. long and 1 mm. thick. For the structure see Figure 105. The powder is light yellowish brown with an odor of ginger and a pungent, slightly bitter taste; starch grains single or 2- to 5-compound, angular or spheroidal, from 3 to 20 microns in diameter, frequently marked by a central cleft; tracheæ with annular or reticulate thickenings of the wall; parenchyma fragments with numerous oil cells.

Asarum contains about 2.5 per cent of volatile oil; a pungent resin; starch; gum; a fragrant principle, asarol; and a small amount of fixed oil. Total ash 6.5 to 9 per cent; acid-insoluble ash about 0.3 per cent.

Asarum is an aromatic stimulant, a carminative and a tonic. Two antibiotic substances have recently been isolated from Asarum, one of which is very active against Gram-positive pus-forming bacteria. Average dose, 2 gm.

Allied Plants.—The rhizome of a related species, *Asarum europæum*, a common plant of the mountainous regions of Europe, is used in the countries in which it grows. It very closely resembles that of *Asarum canadense* and is of a grayish or reddish brown color, with an aromatic and pungent taste, and the powder is sternutatory. It contains 1 per cent of a volatile oil which consists in part of a camphor known as asarin or asaron; tannic acid, colored green with ferric salts; starch; and resin.

POLYGONACEÆ, OR BUCKWHEAT FAMILY

Most of the members of this family are herbaceous plants, with nearly entire leaves, and distinguished by having jointed stems, sheathing united stipules, and a 3- to 4-angled achene. The plants frequently contain tannin cells and resinous secretory cells, the latter sometimes branched. The hairs include both non-glandular and glandular, the head in the latter usually being small, but sometimes large and peltate. Calcium oxalate occurs in the form of rosette aggregates.

RHUBARB

Rhubarb (U. S. P. 1820 to date) consists of the dried rhizome and roots of *Rheum officinale* Baillon or of *Rheum palmatum* Linné or of other species (excepting *Rheum Rhaponticum*) or hybrids of *Rheum*, grown in China or Tibet and deprived of the periderm tissues. *Rheum* comes from the Latin *Rha*, the name of the Volga River near which a species of *Rheum* grows; *palmatum* is in reference to the large, spreading leaves.

The rhizomes are collected in autumn from plants that are eight to ten years old; peeled, perforated, strung on ropes, and dried either in the sun or by artificial heat. The drug is exported chiefly from Shanghai. The principal commercial varieties are known as Chinese rhubarb, Canton rhubarb and Shensi rhubarb, the last-named being preferred.

Rhubarb was known in China as early as 2700 B.C. The *Rha* of the ancient Greeks was possibly Rhapontic rhubarb from near the Black Sea. The Chinese drug may have reached Europe as early as the first

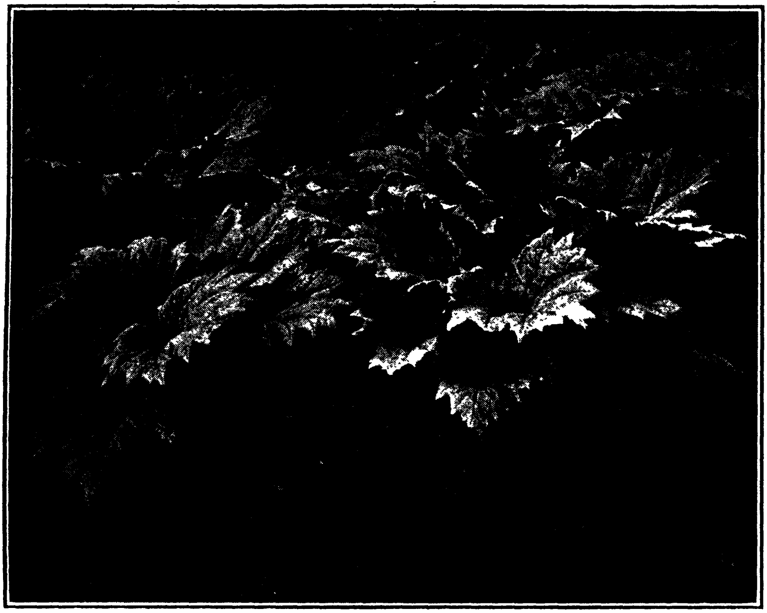


FIG. 106.—*Rheum palmatum* growing in the Medicinal Plant Garden, University of Minnesota.

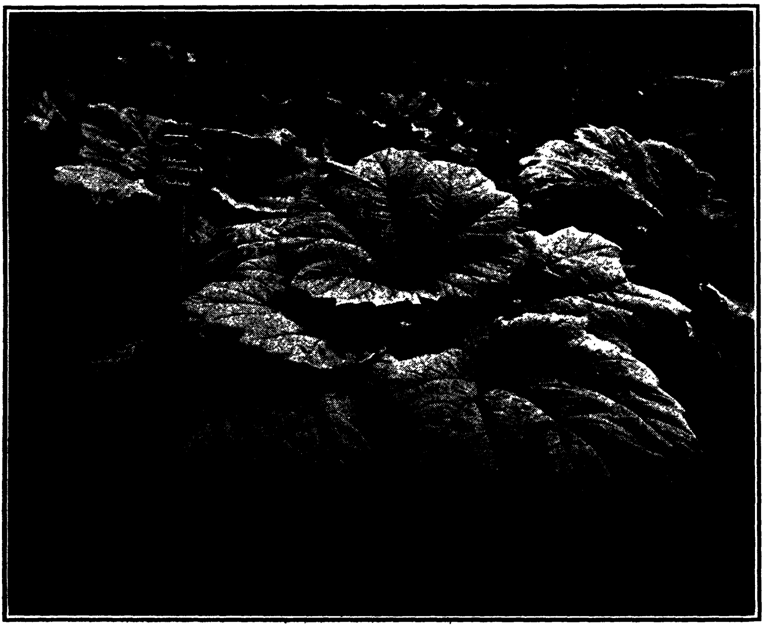


FIG. 107.—*Rheum officinale* growing in the Medicinal Plant Garden, University of Minnesota.

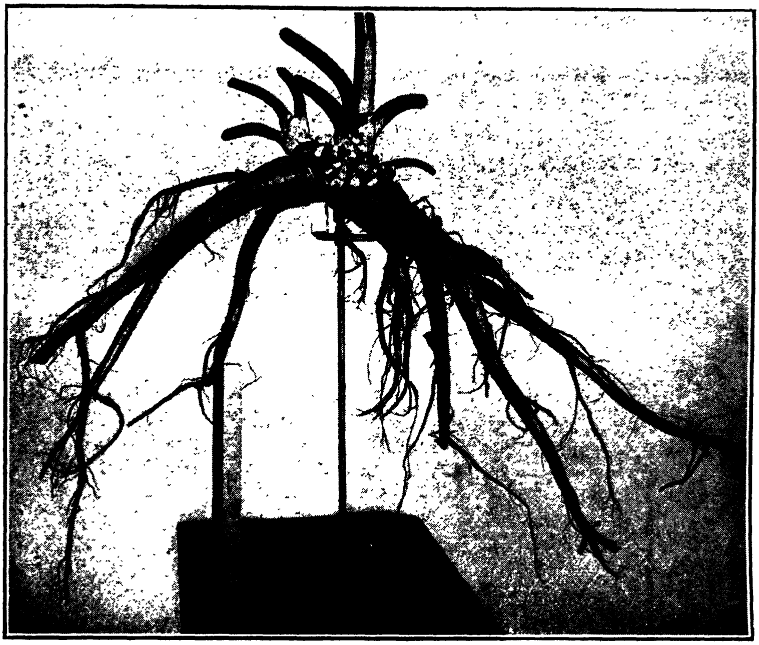


FIG. 108.—*Rheum palmatum* root system, showing typical heavy roots without distinct rhizomes. Medicinal Plant Garden, University of Minnesota.

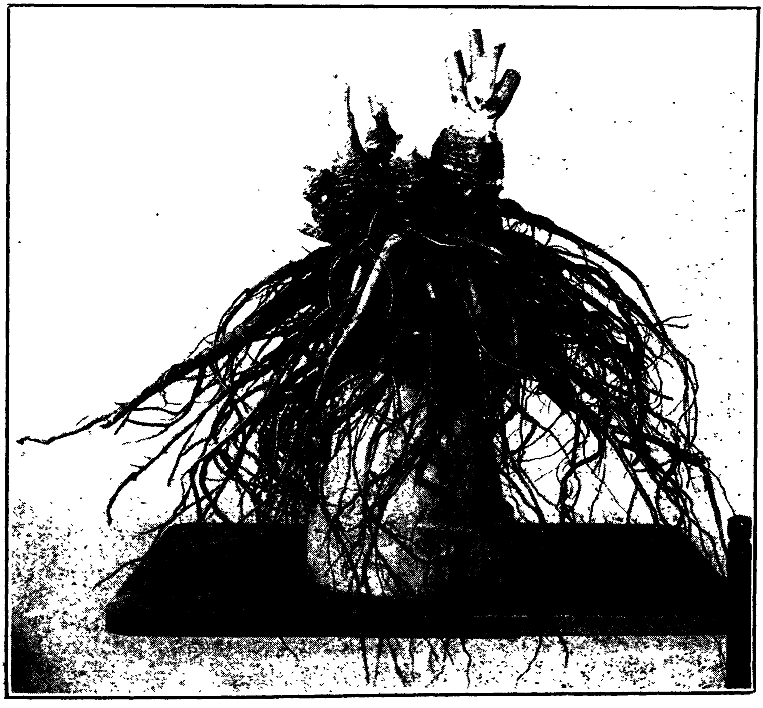


FIG. 109.—*Rheum officinale* root system, showing large distinctive rhizomes and relatively small roots. Medicinal Plant Garden, University of Minnesota.

century A.D. Russia maintained a practical monopoly from about 1650 to near 1800 A.D. by bringing in high quality drug overland from China. Then the drug, frequently of inferior quality, largely came into Europe by sea routes.

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 106, 107, 108, 109, 110, 111 and the U. S. Pharmacopœia.

CONSTITUENTS.—The principal constituents of rhubarb are glucosides of two types: (1) the astringent principles (glucogallin and tetrarin) which yield glucose, gallic acid and other products upon hydrolysis, and (2) the anthraquinone derivatives which yield glucose and hydroxy-methylanthraquinones upon hydrolysis. Rhubarb contains important quantities of emodin and chrysophanic acid; small quantities of rhein and aloe-emodin; gallic acid and catechin; about 7 per cent of calcium oxalate; up to 15 per cent total ash; and about 0.2 per cent acid-insoluble ash.

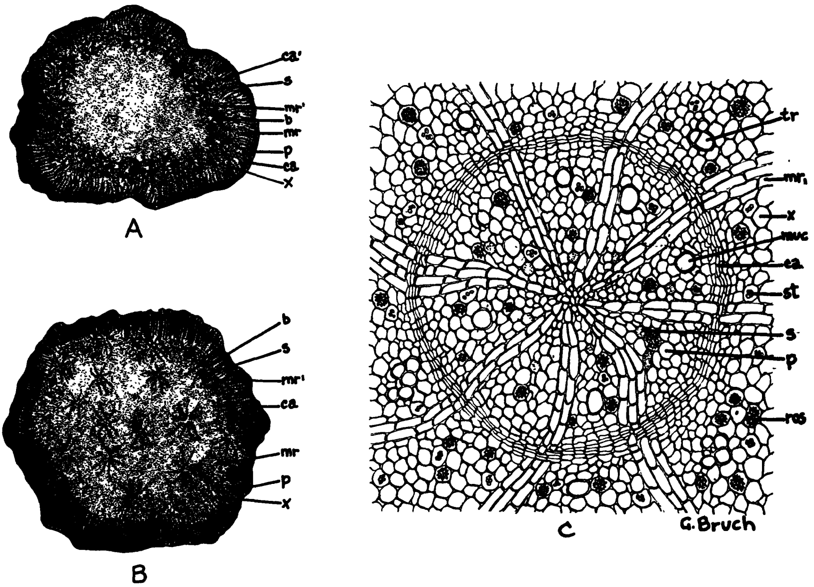


FIG. 110.—Diagrams of transverse sections of (*A*) rhubarb rhizome of the *palmatum* type, and (*B*) rhubarb rhizome of the *officinale* type: *ca*, cambium; *mr*, medullary rays; *p*, phloem; *x*, xylem; *b*, stellate compound vascular bundles, which occur in a continuous ring in the *palmatum* type and more or less irregularly scattered in the *officinale* type. The stellate bundles of the *palmatum* type are relatively smaller than those of the *officinale* type. The stellate bundles show an internal sieve (*s*), cambium (*ca*), medullary rays (*mr*) and an external xylem which merges with the regular xylem. *C*, transverse section through a stellate bundle: *tr*, tracheal tubes; *muc*, mucilage cell; *ros*, rosette aggregates of calcium oxalate (up to 150 microns in diameter); *st*, starch (single or 2- to 3-compound, and up to 25 microns in diameter). (Drawing by Gerston Bruch.)

The anthraquinone compounds may readily be separated from powdered rhubarb by microsublimation (see Figs. 112 and 113).

If low heat is employed the sublimate consists of small needles and prisms, frequently in X-arrangement or rosette formation. Higher temperatures generally result in more or less feathery forms.

If a drop of KOH solution is added to the sublimate the latter dissolves with a red coloration of the solution.

Standards and Tests.—Rhubarb that is light in color, buoyant, or spongy in texture should be rejected. Rhubarb yields not less than 30 per cent of diluted alcohol extractive and not more than 2 per cent of acid-insoluble ash. Rhubarb responds to tests for emodin and chrysophanic acid.

Uses and Dose.—Rhubarb is a laxative, a purgative, a stomachic, an astringent and a tonic. Average dose, 1 gm.

Compound Rhubarb Powder or Gregory's Powder (U. S. P. 1863 to 1936; N. F. 1936 to date) contains powdered rhubarb 25 parts, magnesium oxide 65 parts, and powdered ginger 10 parts, by weight.

Description.—A pinkish mobile powder, becoming darker on exposure to air; the powder contains finely granular magnesium oxide, numerous starch grains and characteristic fragments of vegetable tissues; ginger starch grains are ellipsoidal or ovoid, frequently with a prominent beak, from 5 to 60 microns in diameter; rhubarb starch is in single or compound, spheroidal or polygonal grains, often with a central cleft and up to 25 microns in diameter; mounts made with chloral T.S. strongly effervesce and show more clearly the fragments of reticulate tracheæ and the reddish brown parenchyma of rhubarb, in some of the cells of which occur characteristic rosette aggregate crystals of calcium oxalate up to 150 microns in diameter; with solutions of the alkalis many of the fragments become deep red in color.

Uses and Dose.—Compound Rhubarb Powder is used as an antacid and laxative. Average dose, 2 gm.

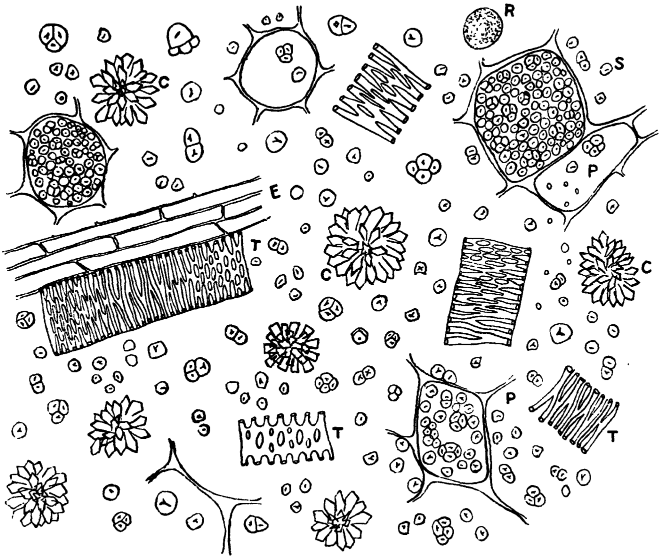


Fig. 111.—Powdered Rhubarb: *C*, rosette aggregates of calcium oxalate, up to 150 microns in diameter; *P*, parenchyma containing starch grains (*S*), from 4 to 25 microns in diameter; *T*, tracheæ; *E*, sieve; *R*, reddish brown amorphous masses separated from the resin or tannin cells.

Adulterants.—Coarse wheat flour, colored with curcurma, has been found in powdered rhubarb, as has also the exhausted drug (the dried marc after preparation of the fluidextract). The latter can be detected by the reduced yield of extractive.

The rhizomes of other species of *Rheum* are also substituted to a limited extent, as rhapontic rhubarb from England or Austria. *Rheum palmatum*, which is cultivated in France, Germany and Russia, produces rhizomes that are lighter in color and less valuable than the Chinese rhubarb, the constituents being similar to those of rhapontic rhubarb.

Rhapontic Rhubarb consists of the peeled rhizomes of *Rheum Rhaponticum*. The drug is more or less cylindrical and distinctly radiate.

Rhapontic rhubarb contains chrysophanic acid and the crystalline glucoside rhaponticin, but contains no emodin, aloe-emodin, or rhein. Rhaponticin is colored purplish red, changing to orange, with sulfuric acid. It is insoluble in ether and readily separates from a dilute alcoholic fluidextract on the addition of ether.

Powdered rhapontic rhubarb responds to the following tests: (1) Boil 10 gm. of the powder for fifteen minutes with 50 cc. of diluted alcohol under a reflux condenser, filter, concentrate to 10 cc., cool, shake with 15 cc. of ether and set the mixture aside for twenty-four hours: crystals of rhaponticin will separate. (2) Shake 0.5 gm. of the powder with 5 cc. of a 2 per cent ammonia solution, keep the mixture at about 30° C. for fifteen minutes, filter into a watch-glass and set aside: crystals of rhaponticin will separate. (3) Examine the powder in filtered ultra-violet light: a marked fluorescence is noted. Official rhubarb responds to none of these tests. A mixture of not less than 25 per cent of rhapontic rhubarb in official rhubarb can be detected by these tests.

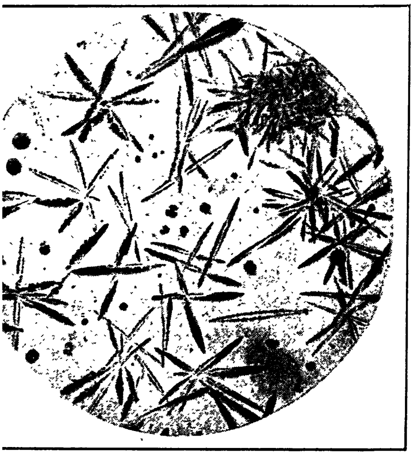


FIG. 112.—Photomicrograph of sublimate from rhubarb at low temperatures.

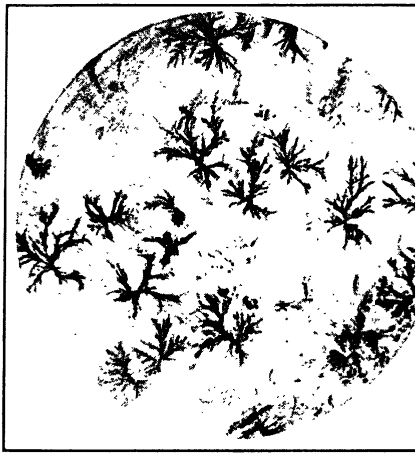


FIG. 113.—Photomicrograph of sublimate from rhubarb at somewhat higher temperature.

Rumex, Yellow Dock, or Curled Dock is the root of *Rumex crispus* or *Rumex obtusifolius*. **Rumex Obtusifolius** and **Rumex Brittanica** were each U. S. P. 1820 to 1863, and then were superseded by **Rumex** U. S. P. 1863 to 1905; N. F. 1916 to 1936.

The drug is collected in the autumn, freed from adhering rootlets, cut into longitudinal pieces or into transverse segments and dried.

The root is nearly simple, slightly tapering, up to 7 cm. in diameter; externally reddish brown or grayish from adhering dust, finely annulate above, deeply wrinkled longitudinally; fracture short and dusty, somewhat fibrous; odor slight; taste astringent and somewhat bitter.

The cortex is thick and consists, along with the central cylinder, of starch-bearing parenchyma; cork of several layers of thin-walled cells and, in *R. crispus*, a few lignified cells beneath the cork; cambium distinct; vascular bundles with few scattered tracheæ and very few fibers.

The powder contains calcium oxalate rosettes up to 65 microns in diameter; numerous ellipsoidal or narrowly elongated, sometimes truncate, starch grains, up to 28 microns in length; a few thin-walled fibers with simple pores; tracheæ up to about 100 microns wide, with scalariform or reticulate thickenings of the wall; and light brown cork cells.

Rumicin, isomeric with chrysophanic acid; nepodin, in greenish prisms; and lapodin, in small needle-shaped crystals may be the active constituents. Total ash about 5.1 per cent with about 0.4 per cent of acid-insoluble ash.

Rumex is an alterative, a laxative and a tonic. Average dose, 4 gm.

Bistorta or English Serpentary is the dried rhizome of *Polygonum bistorta,* a tall perennial herb growing in Europe and Asia. The drug contains from 15 to 20 per cent of gallic acid and yields about 5.5 per cent of total ash and 0.4 per cent of acid-insoluble ash. It is used as a tonic and an astringent. Average dose, 2 gm.

CHENOPODIACEÆ, OR GOOSEFOOT FAMILY

The plants are annual or perennial herbs and are widely distributed. The leaves are mostly alternate and without stipules; the flowers are usually small and of a green color; and the fruit is a 1-seeded utricle. The most prominent characteristic in the structure is the anomalous development of the stem, in which secondary cambiums arise, producing additional vascular bundles at the periphery of those originally formed. A great variety of non-glandular hairs occur. Glandular hairs are rare except in a few genera as *Atriplex* and *Chenopodium,* where occur bladder-like hairs for the storing of water. The **beet,** *Beta vulgaris,* and **spinach,** *Spinacia oleracea,* are important economic plants belonging to this family.

CHENOPODIUM

Chenopodium, or American Wormseed (U. S. P. 1820 to 1905) is the fruit of *Chenopodium ambrosioides* var. *anthelminticum* (Linné) Asa Gray.

Chenopodium Oil or Oil of American Wormseed (U. S. P. 1820 to 1947; N. F. 1947 to date) is the volatile oil distilled with steam from the fresh, flowering and fruiting, overground parts of *Chenopodium ambrosioides* var. *anthelminticum* (Linné) Asa Gray. The plant is indigenous to the West Indies but naturalized in the United States. It is extensively cultivated in Carrol County, Maryland, the oil distilled from plants in that locality being known as Baltimore Oil. If the plants are grown for the fruits they are allowed to mature, but when grown for the oil they are harvested while the tops are still green and immediately distilled. The oil is formed in glandular hairs (see Fig. 115), occurring on the leaves, flowers and fruits, but being particularly abundant on the pericarp and ovary. The yield of oil is from 1 to 2 per cent of the partially dried herb.

Properties.—Chenopodium fruit is about 2 mm. in diameter, irregularly globular, glandular, of a dull green color, an aromatic, somewhat terebinthenate, characteristic odor, and a bitterish pungent taste. The oil is a colorless or pale yellow liquid, having a peculiar disagreeable odor and a bitter, burning taste; specific gravity not less than 0.950 at 25° C.; refractive index between 1.4740 and 1.4790 at 20° C., and is soluble in not less than 8 volumes of 70 per cent alcohol.

Constituents.—Ascaridol, 60 to 80 per cent; *p*-cymene about 20 per cent; *l*-limonene and *d*-camphor. Ascaridol, the active principle, is an organic peroxide, liable to explode when heated.

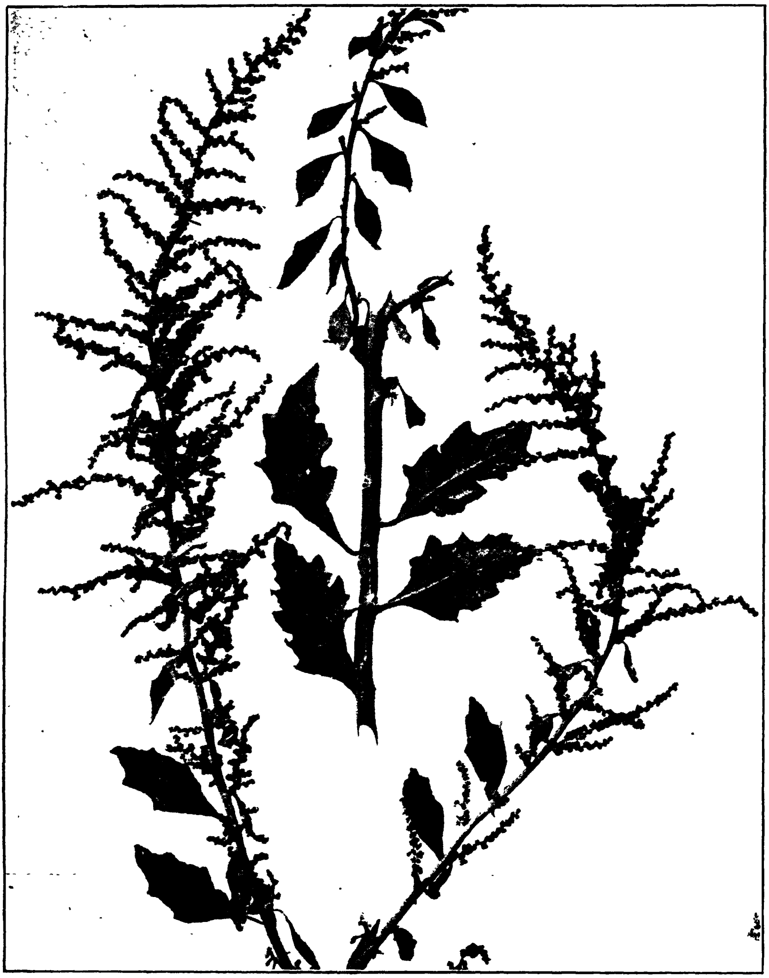


Fig. 114.—American Wormseed. Fruiting branches of *Chenopodium ambrosioides* var *anthelminticum*. (From U. S. Department of Agriculture.)

Standards.—Oil of chenopodium contains not less than 65 per cent by weight of ascaridol. For other tests and constants see the National Formulary.

Uses and Dose.—An anthelmintic, especially for round worms but also for hook worms and intestinal amœbæ. Average dose: Chenopodium, 2 gm.; Chenopodium Oil, in single adult doses as an anthelmintic, 1 cc.

Allied Drugs.—**Mexican Tea** is official in some foreign pharmacopœias. It consists of the above ground portion of *Chenopodium ambrosioides*, a plant resembling and very closely related to *Chenopodium ambrosioides* var. *anthelminticum*, and widely distributed in the United States. It yields about 0.3 per cent of a volatile oil which is used in Brazil as an anthelmintic.

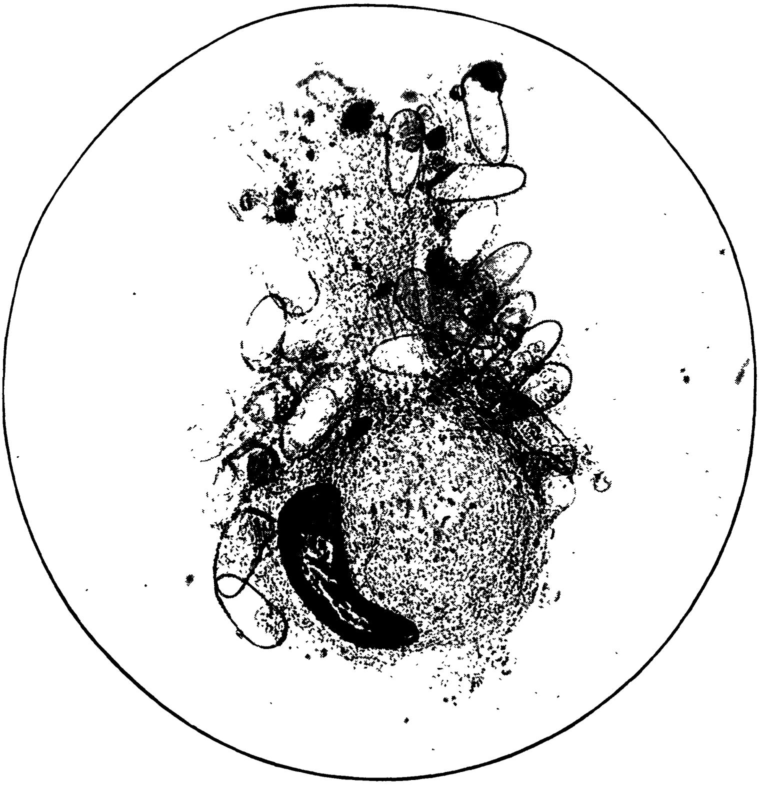


Fig. 115.—Photomicrograph of a single pistil of *Chenopodium* just previous to pollination showing the numerous glandular hairs which in the normal state form a dense ring-like cluster on the upper half of the ovary. These hairs become detached in the mechanical preparation of the mount. (Photo by Hogstad.)

PHYTOLACCACEÆ, OR POKEWEED FAMILY

The family includes herbs, shrubs and trees and comprises less than 100 species. They are for the most part indigenous to tropical and subtropical America and Africa, being represented in the United States by one genus, *Phytolacca*. The structure of the root is anomalous, consisting of the formation of successive secondary rings of vascular bundles. The hairs are of the simple, uniseriate type. Neither glandular hairs nor special secretory cells occur in plants of this family.

Phytolacca, or Poke Root (U. S. P. 1820 to 1916; N. F. 1916 to 1947) is the dried root of *Phytolacca americana* Linné, a perennial herb indigenous to eastern North America, and naturalized in the West Indies and southern Europe. The generic name *Phytolacca* means "red plant" and refers to the red juice from the berries. The root is collected in autumn and, after removal of the rootlets, is cut into transverse and longitudinal pieces and dried.

Phytolacca root externally is yellow-brown, thickly annulate with light-colored, low, transverse ridges. Internally it is very light brown, the transverse slices characterized by alternating zones of collateral fibrovascular bundles and parenchyma, formed by secondary cambiums (see Fig. 117). The powdered drug is light yellow to brownish; sternutatory and acrid; starch is in simple or compound grains, the individual grains up to 35 microns in diameter; calcium oxalate is in sphenoidal microcrystals or raphides up to 50 microns in length; long sclerenchymatous fibers associated with large scalariform tracheæ are numerous.

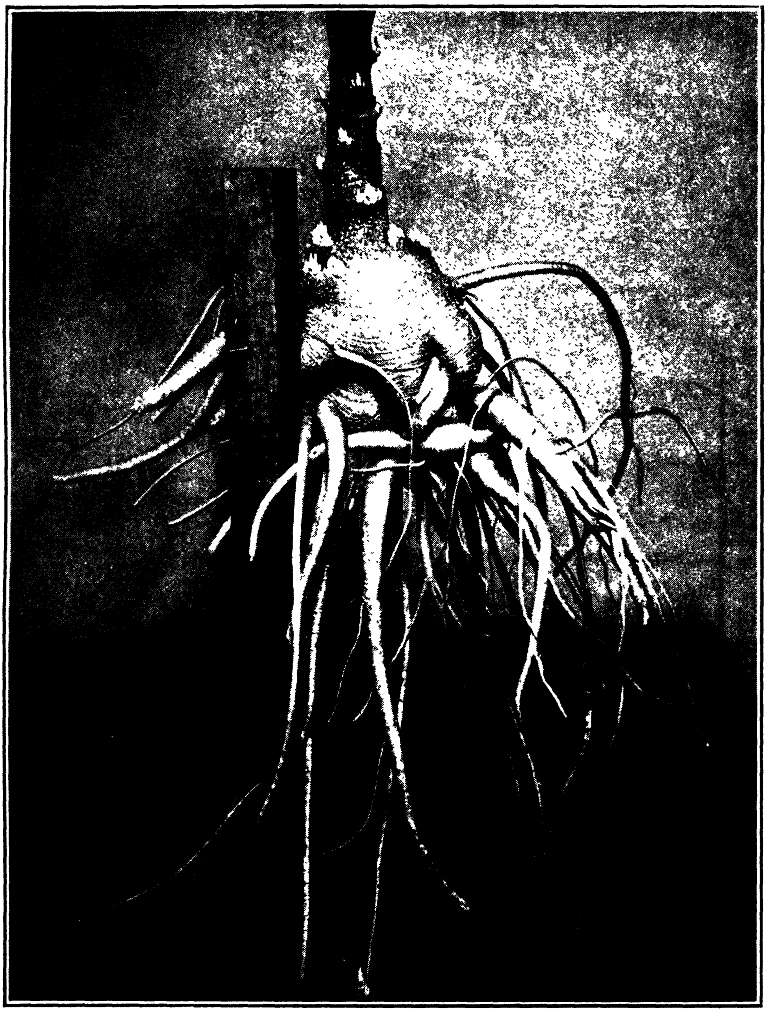


Fig. 116.—*Phytolacca americana*. Root system of one-year-old plant. Medicinal Plant Garden, University of Minnesota.

Phytolacca Fruit or Poke Berries (U. S. P. 1820 to 1905) occur in agglutinated masses of a purplish black color, and consist of the compound berries, which are about 8 mm. in diameter and composed of 10 loculi, each of which contains a single, lenticular, black seed. The sarcocarp is fleshy, sweet and slightly acrid, and contains a purplish red coloring principle which is soluble in water but not in alcohol, and which is decomposed on heating the aqueous solution.

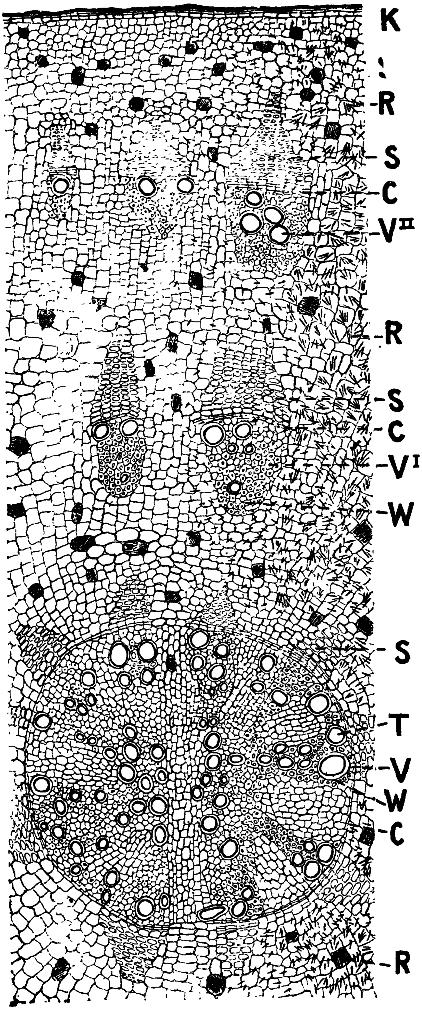


Fig. 117.—Transverse section of phytolacca root, showing the fibrovascular bundles (*V*, V^{I}, V^{II}) which are produced by distinct cambiums (*C*). The parenchyma contains little starch, and some of the cells (*R*) show short raphides of calcium oxalate, many of the crystals being distributed in the section. The cork (*K*) is thin except at the ridges, where it is much thickened; the wood bundle consists of sieve (*S*), wood fibers (*W*) and traehcæ (*T*).

The fruit also contains phytolaccic acid, several fruit acids and phytolaccin, a substance resembling tannin.

Phytolacca contains a bitter, saponin-like glucoside; a crystalline alkaloid, phytolaccine, which is soluble in alcohol and sparingly soluble in water; phytolaccic acid; formic acid; potassium formate; total ash about 8.5 per cent, of which about one-half is potassium oxide; acid-insoluble ash about 0.5 per cent.

Phytolacca is an alterative, an emetic and a purgative. Average dose: emetic, 1 gm.; alterative, 0.1 gm.

RANUNCULACEÆ, OR CROWFOOT FAMILY

This is a large family, consisting of about 1200 species, widely distributed except in the tropics. They are mostly annual or perennial herbs, a few being somewhat woody and climbing, as *Clematis*. The parts of the flower are numerous, the sepals and petals being from 3 to 15, the stamens indefinite, and the carpels usually 5 to 20. The fruits are either achenes, follicles or berries. In transverse sections the xylem of the collateral vascular bundle is heart-shaped, having the phloem distributed in the sinus. The pericycle, especially in the woody species, is in the form of a closed ring of sclerenchyma. The hairs are both glandular and non-glandular, the former being always 1-celled and usually mucilaginous. In the leaves of *Aconitum* and *Anemone*, so-called "arm cells" occur in the palisade layer.

ACONITE

Aconite or Monkshood (U. S. P. 1851 to 1942; N.F. 1942 to date) is the dried tuberous root of *Aconitum napellus* Linné. *Aconitum* is from the Greek, meaning "without soil" and refers to the plant growing on stony ground; *napellus* is from the Latin, meaning "little turnip" and refers to the shape of the root.

The plant is a perennial herb with a fusiform tuberous root from which arise one or more lateral shoots which develop into conical daughter tubers. The plant may be propagated from the daughter tubers. There are about 60 species of *Aconitum* which differ widely from one another in constituents and which readily hybridize; hence only the official species should be propagated for drug. The drug is preferably gathered at the flowering stage, though in the fall the aconitine content also appears to be high; the flower offers the best means for differentiating species. The drug is collected in Germany and Switzerland from wild plants, and in England from cultivated plants, and carefully dried. The poisonous nature of *Aconitum* was known to the ancient Chinese and Indians. Of the eighteen varieties of aconite mentioned by Hindu writers, ten were considered too poisonous to be used in medicine. Its poisonous nature was well known in mediæval times, but Störch, a Viennese physician, introduced it into medicine in 1762.

Description, Structure and Powder.—See Figures 118, 119, and the National Formulary.

Constituents.—Aconitine, a crystalline alkaloid, up to 0.75 per cent; it readily hydrolizes into benzoylaconine and aconine, both of which are amorphous. Aconine is much less toxic than, and apparently produces physiological effects contrary to those of aconitine. The hydrolysis of aconitine may be expressed by the following equations:

$$\underset{\text{Aconitine}}{C_{34}H_{47}O_{11}N} + H_2O \rightarrow \underset{\text{Benzoylaconine}}{C_{32}H_{45}O_{10}N} + \underset{\text{Acetic acid}}{CH_3.COOH}$$

$$\underset{\text{Benzoylaconine}}{C_{32}H_{45}O_{10}N} + H_2O \rightarrow \underset{\text{Aconine}}{C_{25}H_{41}O_9N} + \underset{\text{Benzoic acid}}{C_6H_5.COOH}$$

Amorphous aconitine (mild aconitine) consists of a mixture of alkaloids or decomposition products from aconite. It is about one-tenth as toxic as crystalline aconitine.

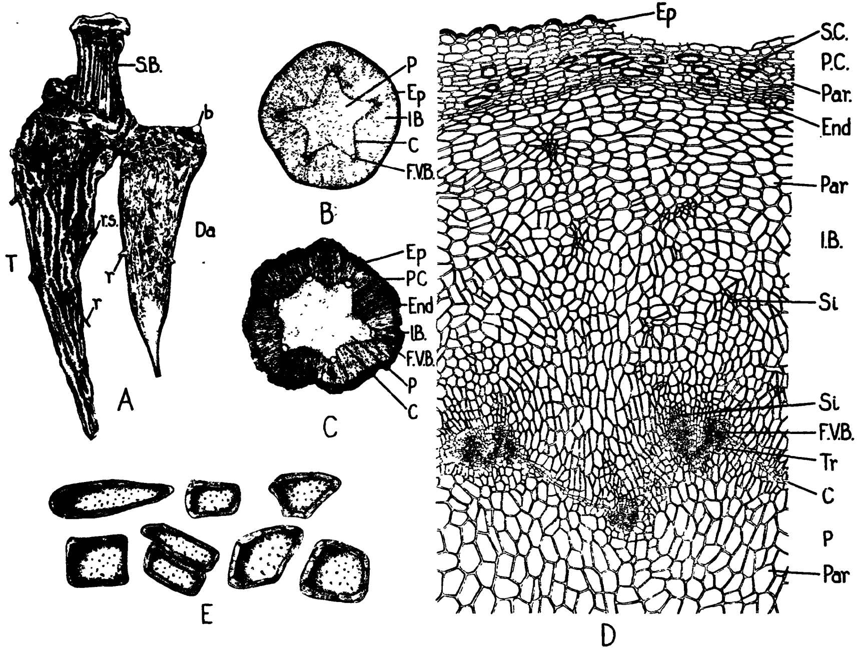


FIG. 118.—*Aconitum napellus*. *A*, tuberous root (*T*) with attached daughter tuber (*Da*) (these are conical, smooth or longitudinally wrinkled, externally dark brown or grayish brown, from 4 to 10 cm. in length and from 1 to 3 cm. in diameter at the crown), showing stem-base (*sb*), bud (*b*), root-scars (*rs*), or short rootlets (*r*). *B*, lens view of a transverse section of a young tuberous root; *C*, lens view of a transverse section of an older tuberous root; and *D*, more highly magnified view of the transverse section of the tuberous root. Epidermis (*Ep*); primary cortex (*pc*) consisting of parenchyma (*Par*) with scattered characteristic stone cells (*sc*); modified endodermis (*End*); inner bark (*IB*) of parenchyma (*Par*) with scattered islets of sieve tissue (*Si*); 5- to 8-angled cambium (*c*), with a 2- to 4-rayed collateral fibrovascular bundle (*FVB*) containing sieve (*Si*) and tracheal tubes (*Tr*) in each angle; pith (*P*) consisting of parenchyma (*Par*). *E*, typical rectangular or elongated stone cells from the primary cortex. These stone cells are from 100 to 400 microns in length. (Drawing by Bernard Marder.)

Aconitine (U. S. P. 1851 to 1882, 1905 to 1936; as a reference standard, U. S. P. 1936 to 1942; N. F. 1936 to date) is an alkaloid obtained from aconite.

It appears as colorless or white crystals, odorless and stable in air. It is extremely poisonous and should not be tasted. It melts at 197° to 198° C., after preheating to 180° C.; it is slightly soluble in water and readily soluble in alcohol, ether or benzene. An aqueous solution of the alkaloid, after acidulating with acetic acid, gives on the addition of a solution of potassium permanganate, a red crystalline precipitate; phosphomolybdic acid, potassium mercuric iodide and tannin give white precipitates; phosphoric acid gives a violet color reaction; and vanadic acid an orange reaction. Many species of *Aconitum* contain toxic aconitines, while others contain the less toxic aconines. Aconitine of high purity is used as a reference standard in the official assay of aconite.

STANDARDS.—Aconite possesses a potency, per cubic centimeter of tincture, equivalent to not less than 0.15 mg. of reference aconitine.

An unofficial qualitative test having some quantitative value in determining the potency of powdered aconite is as follows: 0.5 gm. of the finely powdered aconite is mixed with 500 cc. of water and shaken occasionally during the course of five minutes. A few cubic centimeters of the filtered solution, if swallowed, produces a distinct and characteristic sensation in the throat.

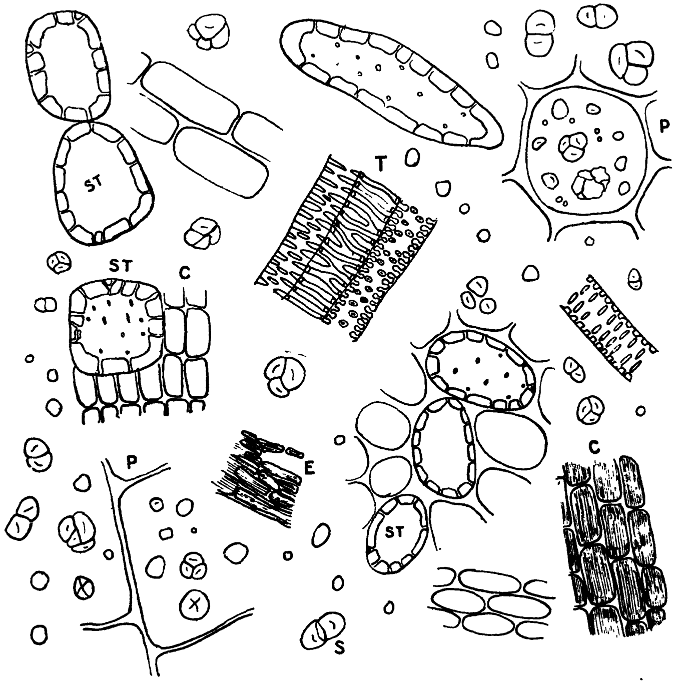


FIG. 119.—Powdered Aconite. Starch grains (*S*) numerous, spheroidal, somewhat plano-convex, single or 2- to 5-compound, the individual grains from 3 to 20 microns in diameter and frequently with a central cleft; tracheæ (*T*) mostly with slit-like, simple pores, sometimes with spiral or reticulate thickenings or with bordered pores; stone cells (*St*) single, tabular, irregular in shape or elongated to fibers from 100 to 400 microns in length, walls from 8 to 25 microns in thickness, strongly lignified and having large simple pores; fragments of cork (*C*, *E*) few, yellowish brown; fragments of parenchyma (*P*) numerous, the cells being filled with starch grains; bast fibers from stems few, very long, with lignified walls about 5 microns in thickness, and marked by transverse or oblique, slit-like pores.

USES AND DOSE.—Aconite is a heart and nerve sedative; locally in the form of a tincture, it is used as an analgesic. Average dose, 0.06 gm.

Aconite Leaves (U. S. P. 1820 to 1882) consists of the leaves and flowering tops of *Aconitum napellus*. The drug should be protected against air and light after gathering and careful drying.

It occurs more or less crumpled or broken; entire leaves long petiolate, and palmately divided into 3 to 7 segments; each with 2 or 3 deeply incised lobes which are linear and acutely pointed. The flowers are dark blue, usually in a spike-like raceme, the upper sepal being hooded or helmet-shaped and covering the 2 long-clawed smaller petals; fruit of 2 or 3 separate somewhat flattened lanceolate follicles and enclosing several seeds.

The powder is dark yellowish green; with numerous fragments showing wavy walled epidermal cells and elliptical stomata. Fragments of the blue sepals are colored purplish red upon the addition of hydrochloric acid, and bright green upon the addition of solutions of the alkalis.

The drug contains aconitine from 0.15 to 0.3 per cent; aconitic acid, tannic acid, inosite and sugar; ash yield from 15 to 20 per cent. Aconite leaves have the same, though weaker, actions as aconite root.

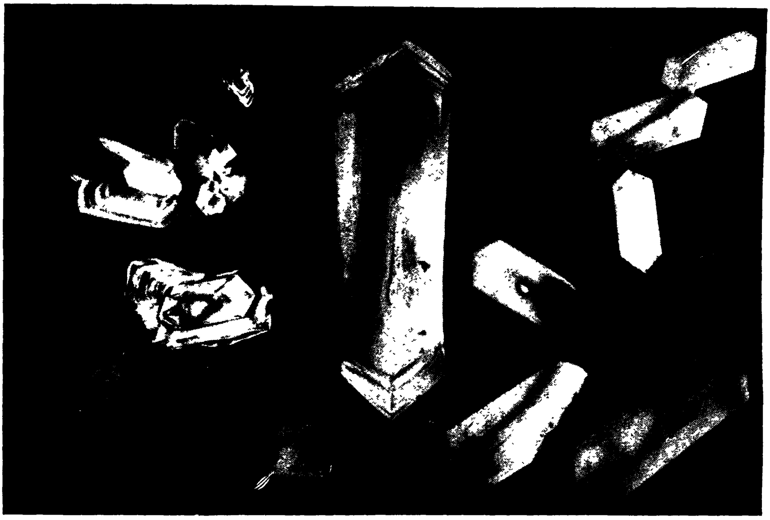


Fig. 120.—Aconitine: orthorhombic crystals, crystallized from alcoholic solutions.

Allied Drugs.—**Japanese Aconites.**—Two aconites appear in commerce under this designation, one derived from *Aconitum fischeri* having a conical root smaller and less wrinkled than the official drug, and the other derived from *Aconitum uncinatum* var. *japonicum*, which is shorter and plumper than the official drug. The former contains japaconitine, which upon hydrolysis yields acetic and benzoic acids and japaconine; the latter contains jesaconitine which upon hydrolysis yields acetic and anisic acids and jesaconine.

Indian Aconites.—Several aconites native to India are occasionally found in commerce, the most common from *Aconitum ferox, Aconitum balfourii, Aconitum laciniatum* and *Aconitum deinorhizum.* The roots of these species are considerably larger (up to 15 cm. in length and 4 cm. in diameter at the crown) and the starch is more or less gelatinized from excessive heating during drying. The roots contain pseudoaconitine which, upon hydrolysis, yields acetic and veratric acids and pseudoaconine. Other Indian varieties include *Aconitum chasmanthum,* a very small root (up to 2 cm. long) containing indaconitine which upon hydrolysis yields acetic and benzoic acids and pseudoaconine; *Aconitum spicatum* containing bikhaconitine which yields acetic and veratric acids and bikhaconine; and *Aconitum heterophyllum* containing the alkaloid atisine which is much less toxic than the aconitines. **Other Aconites** include *Aconitum stærckianum,* a native of the Alps, the conical roots of which often occur in clusters of three or four, and contain aconitine. *Aconitum lycoctonum* is a yellow-flowered European species having a several-headed rhizome and contains lycaconitine.

HYDRASTIS

Hydrastis or Golden Seal (U. S. P. 1831 to 1842, 1863 to 1936; N. F. 1936 to date) consists of the dried rhizome and roots of *Hydrastis canadensis* Linné.

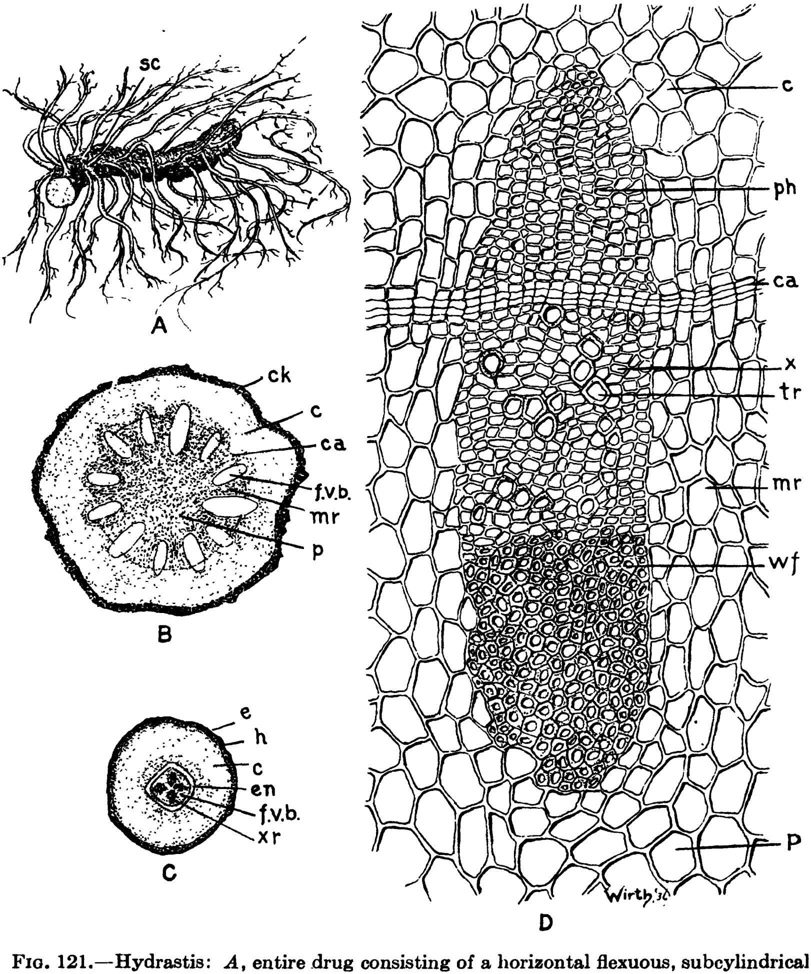


FIG. 121.—Hydrastis: *A*, entire drug consisting of a horizontal flexuous, subcylindrical rhizome, 1 to 5 cm. long and 2 to 10 mm. in diameter, more or less annulate and wrinkled longitudinally; yellowish brown to dark grayish brown; marked by stem-scars (*sc*) and numerous roots or short root protuberances; fracture short and waxy; internally deep yellow or grayish yellow. Roots (*r*) numerous, up to 35 cm. in length and up to 1 mm. in diameter, more or less curved and twisted and usually matted together; fracture short and brittle. Odor distinctive and taste bitter. *B*, lens view of a transverse section of the rhizome showing a several-rowed cork (*ck*), a cortex (*c*) of about 25 rows of thin-walled parenchyma, 12 to 20 radially elongated fibrovascular bundles (*fvb*) separated by broad medullary rays (*mr*); cambium (*ca*); large pith (*p*). *C*, lens view of a transverse section of the root showing epidermis (*e*), hypodermis (*h*), cortex (*c*), endodermis (*en*) and a central fibrovascular bundle (*fvb*) with 2 to 6 xylem rays (*xr*). *D*, transverse section through one of the fibrovascular bundles of the rhizome showing cortex (*c*), phloem (*ph*), cambium (*ca*), xylem (*x*) with tracheæ (*tr*) and wood fibers (*wf*), medullary ray (*mr*), and pith (*p*). (Drawings by Wirth.)

Hydrastis is from the Greek meaning "to accomplish or act with water;" the specific name refers to the habitat. The plant is a perennial herb with a short horizontal rhizome bearing numerous long, slender roots. Golden seal was plentiful in the forests of the eastern United States and Canada, but in recent years has become almost extinct, due to ruthless collection because of its relatively high market price. It is still collected from wild plants to some extent in the Ohio River Valley, and is cultivated in Oregon, Washington, North Carolina, Tennessee, Michigan, Wisconsin and other localities. The plants, propagated from rhizome buds, require from three to four years to produce marketable drug. It is gathered in autumn, the terminal buds replanted and the drug carefully dried. Hydrastis was known to the Cherokee Indians, who used it as a dye as well as an internal remedy, and who introduced its use to the early American settlers.

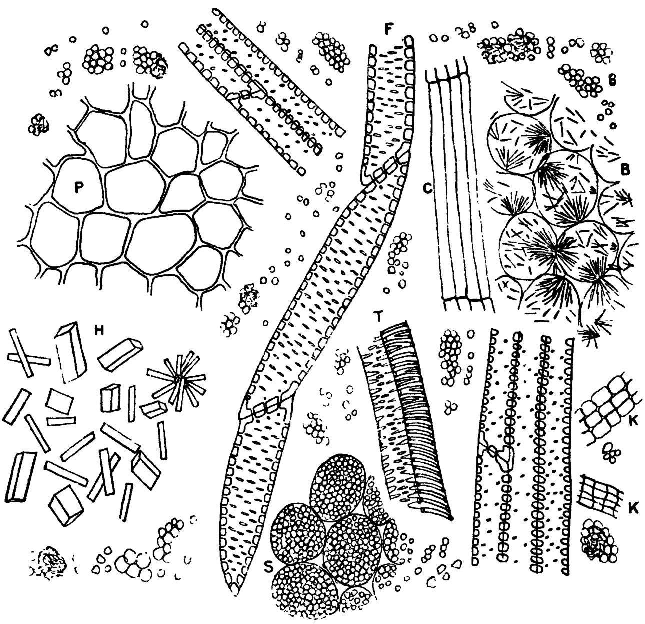


FIG. 122.—Powdered Hydrastis: *P*, parenchyma; *S*, parenchyma containing numerous starch grains 2 to 15 microns in diameter, mostly simple and nearly spheroidal, but occasionally 2- to 6-compound; *T*, tracheæ with bordered pores or occasionally spiral, annular or reticulate thickenings of the walls; *F*, fibers with simple pores and from 200 to 300 microns long; *C*, cambium; *K*, cork; *B*, parenchyma cells showing the separation of acicular crystals of one of the alkaloids which occurs on the addition of concentrated sulfuric acid; *H*, prisms of one of the alkaloids which separate on the addition of concentrated sulfuric acid to a powder previously moistened with water.

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 121, 122, and the National Formulary.

CONSTITUENTS.—Three alkaloids have been isolated from hydrastis; hydrastine, berberine and canadine; of these, hydrastine (1.5 to 4 per cent) is the most important.

Hydrastine (U. S. P. 1905 to 1926) is readily soluble in chloroform, alcohol and ether, but almost insoluble in water. It crystallizes in prisms, melting at 131° to 132° C. On treatment with nitric acid hydrastine undergoes hydrolytic oxidation yielding opianic acid and hydrastinine, which has been recognized in the Pharmacopœia as **Hydrastinine Hydrochloride** (U. S. P. 1894 to 1926) which occurs in light yellow needles or powder, very soluble in water or alcohol, but much less so in chloroform or ether.

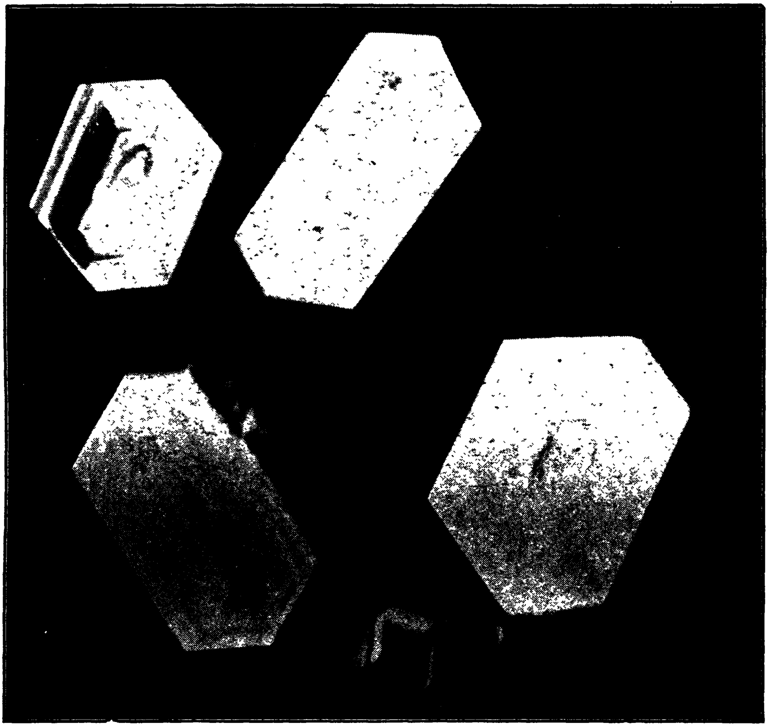


FIG. 123.—Hydrastine: large, nearly equidimensional orthorhombic crystals from alcoholic solution.

Hydrastine Hydrochloride (U. S. P. 1916 to 1926; N. F. 1926 to date) occurs as a white or creamy white powder, odorless, bitter and hydroscopic. It is readily soluble in water or alcohol, but slightly so in chloroform or ether.

Berberine is readily soluble in water but almost insoluble in ether. The salts of berberine form bright yellow crystals. Berberine sulfate crystallizes in needles melting at 144° C.

l-**Canadine** is insoluble in water but readily soluble in alcohol, chloroform and ether. It crystallizes in needles melting at 134° C.

These alkaloids may be obtained by microsublimation or by microextraction and may be identified by means of microcrystalline reactions. Mounting the powder in sulfuric acid results in the formation of acicular crystals of the alkaloidal sulfates, this latter reaction being employed as an identity test for hydrastis (see Figs. 123 and 124).

STANDARDS.—Hydrastis yields not less than 2.5 per cent of the anhydrous ether-soluble alkaloids of hydrastis. It contains not more than 4 per cent of foreign organic matter, and yields not more than 3 per cent of acid-insoluble ash.

USES AND DOSE.—Hydrastis is a bitter tonic and an astringent used in inflammation of the mucous membrane. Hydrastine and Hydrastinine salts are internal hemostatics. Berberine salts are antiperiodic, stomachic, and tonic. *l*-Canadine paralyzes the central nervous system and causes severe peristalsis. Average dose, of the drug, 2 gm.; of hydrastine, 100 mg.; of hydrastinine hydrochloride, 0.3 gm.; of berberine sulfate as stomachic and tonic, 45 mg., as antiperiodic, 0.6 gm.

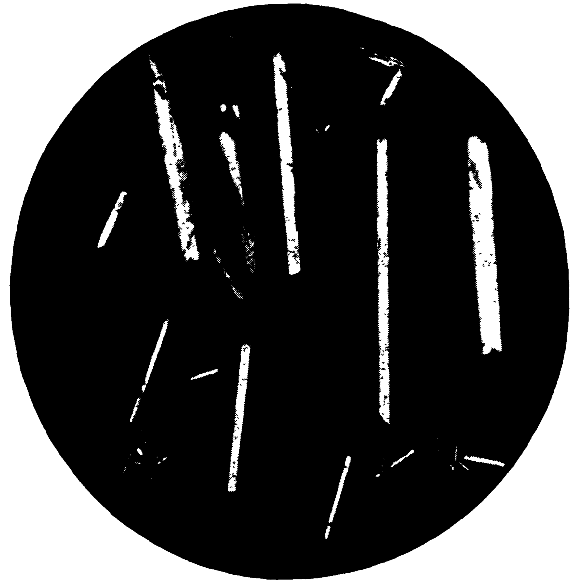


FIG. 124.—Berberine sulfate: orthorhombic crystals from aqueous solution.

ALLIED PLANTS.—The alkaloid berberine, or a principle closely resembling it, is found in the following plants of the *Ranunculaceæ;* False rhubarb (*Thalictrum flavum*) of Europe; and the following plants growing in the United States: gold-thread (*Coptis trifolia*), yellow root (*Zanthorhiza apiifolia*), and marsh marigold (*Caltha palustris*). A principle resembling berberine is found in the following plants belonging to the *Rutaceæ:* several species of *Zieria* found in southern Australia and Tasmania, and *Toddalia aculeata* found in the mountains of eastern Africa, tropical Asia and the Philippine Islands. (Also see Berberis.)

CIMICIFUGA

Cimicifuga, Black Cohosh, Black Snakeroot or Macrotys (U. S. P. 1820 to 1936; N. F. 1936 to date) consists of the dried rhizome and roots of *Cimicifuga racemosa* (Linné) Nuttall.

The generic name *Cimicifuga* means in Latin "to drive away bugs," in reference to its insect poisonous properties; *racemosa* refers to the flowers in racemes or clusters.

The plant is a perennial herb growing in eastern North America. The drug is collected in the autumn, most of the commercial supply coming from the Blue Ridge Mountains.

DESCRIPTION.—Rhizome horizontal, with numerous upright or curved branches and few roots; externally dusky brown to dark yellowish brown, slightly annulate from circular scars of bud-scales, the upper surface with buds, stem-scars and stem remnants, the lower and lateral surfaces with numerous root-scars and few roots; fracture horny; internally, dark brown and waxy or sometimes whitish and mealy; bark about 1 mm. in thickness, wood 4 to 5 mm. in thickness, and distinctly radiate, pith 3 to 5 mm. in diameter.

Roots brittle, nearly cylindrical or obtusely quadrangular; longitudinally wrinkled; 1 to 3 mm. in diameter; fracture short; internally, wood usually 4-rayed.

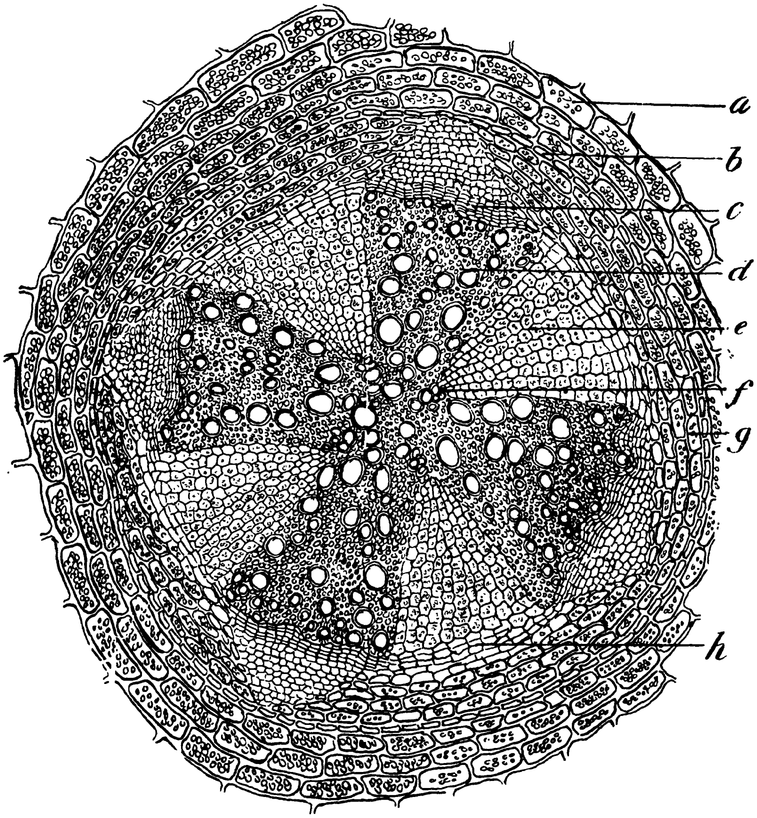


FIG. 125.—Cimicifuga. Transverse section of the central part of a mature root in which the secondary changes are completed: *a*, parenchyma; *b*, endodermis; *c*, cambium zone; *d*, tracheæ in secondary xylem; *e*, broad, wedge-shaped medullary rays; *f*, outer portion of one of the primary xylem bundles; *g*, parenchyma beneath the endodermis; *h*, interfascicular cambium. (After Bastin.)

POWDER.—Pale to moderate yellow brown; odor slight; taste bitter and acrid; starch grains numerous, simple or compound, the individual grains from 3 to 15 microns in diameter, spheroidal or more or less polygonal, each with a somewhat central cleft; fragments of tracheæ with sclariform thickenings or bordered pores; wood fibers numerous, thin-walled, strongly lignified; irregular, yellowish brown fragments of suberized epidermis of tabular cells, sometimes elongated, and with walls considerably thickened. (Also see Fig. 125 and the National Formulary.)

Constituents.—Four crystalline principles: two soluble in chloroform, one in ether, and one in water; a trace of an alkaloid and several organic acids; considerable starch and a tannin-like principle giving a green color with ferric salts, thus distinguishing the drug from the rhizome of *Helleborus niger;* acid-insoluble ash not exceeding 4 per cent. **Macrotin or cimicifugin** is a mixture of the resinous constituents, precipitated by adding the alcoholic extract to water.

Uses and Dose.—Cimicifuga is an alterative, a sedative and an emmenagogue. Its use is empirical. Average dose, 1 gm.

LARKSPUR

Larkspur (U. S. P. 1820 to 1882; N. F. 1916 to 1926 [*D. Consolida*]; N. F. 1916 to date [*D. Ajacis*]) is the dried ripe seed of *Delphinium Ajacis* Linné. The generic name *Delphinium* is from the Greek, meaning "dolphin," so-called because the nectary resembles the figure of a dolphin; *Aiacis* is after Ajax; *Consolida* refers to its supposed power to heal or consolidate wounds.

The plants are annuals, indigenous to central Europe and widely cultivated in America as garden plants. The drug is imported from Europe. Delphinium seeds were employed by the Greeks and Romans as emetics and cathartics, but due to their poisonous nature their internal use has long since been discontinued.

Description, Structure and Powder.—See the National Formulary. The seed of *Delphinium Consolida* differ from those of *D. Ajacis* in that the rows of tangentially elongated epidermal cells are scalloped or form scale-like projections and slant toward the base of the seed and the cells are smaller, up to about 30 microns in width and 350 microns in length.

Constituents.—The principal constituent is the alkaloid delphinine, which crystallizes in rhombic prisms and resembles aconitine in its physiological properties.

Standards.—Larkspur contains not more than 2 per cent of foreign organic matter, and yields not more than 2 per cent of acid-insoluble ash.

Uses.—Delphinium is used externally in the form of a tincture as a parasiticide.

Staphisagria (U. S. P. 1882 to 1926) is the dried ripe seed of *Delphinium Staphisagria,* an annual or biennial native of southern Europe and Asia Minor, and cultivated in Austria (Trieste), Italy and southern France, from where the commercial supplies are obtained.

The seed is anatropous, irregularly triangular or somewhat tetrahedral, one side convex, the others plane, the micropylar end acute or obtuse; 5 to 6 mm. in length, 3 to 6 mm. in breadth; externally dark brown, becoming grayish with age; more or less uniformly reticulate, the pits being about 0.5 mm. in diameter, raphé forming a more or less distinct ridge on the largest of the plane surfaces or on the edge of two united sides; inner seed coat yellowish brown; the endosperm white or yellowish, and enclosing at the pointed end a small, straight embryo; slightly odorous; taste of endosperm intensely bitter and acrid.

Sections show an epidermal layer of yellowish, nearly tabular, thick-walled, non-lignified cells, some being extended outward as papillæ, and forming the reticulations of the seed coat; 2 or 3 rows of parenchyma cells with more or less irregular thin walls; a thin layer of very small, thick-walled cells with numerous, lattice-like or reticulate pores; endosperm large, composed of polygonal cells enclosing small aleurone grains and fixed oil, the latter forming in large globules on the addition of solutions of hydrated chloral, the alkalies or sulfuric acid.

The powder is grayish-brown or light brown.
Staphisagria contains delphinine and staphisagroine.
Staphisagria is used as a parasiticide.

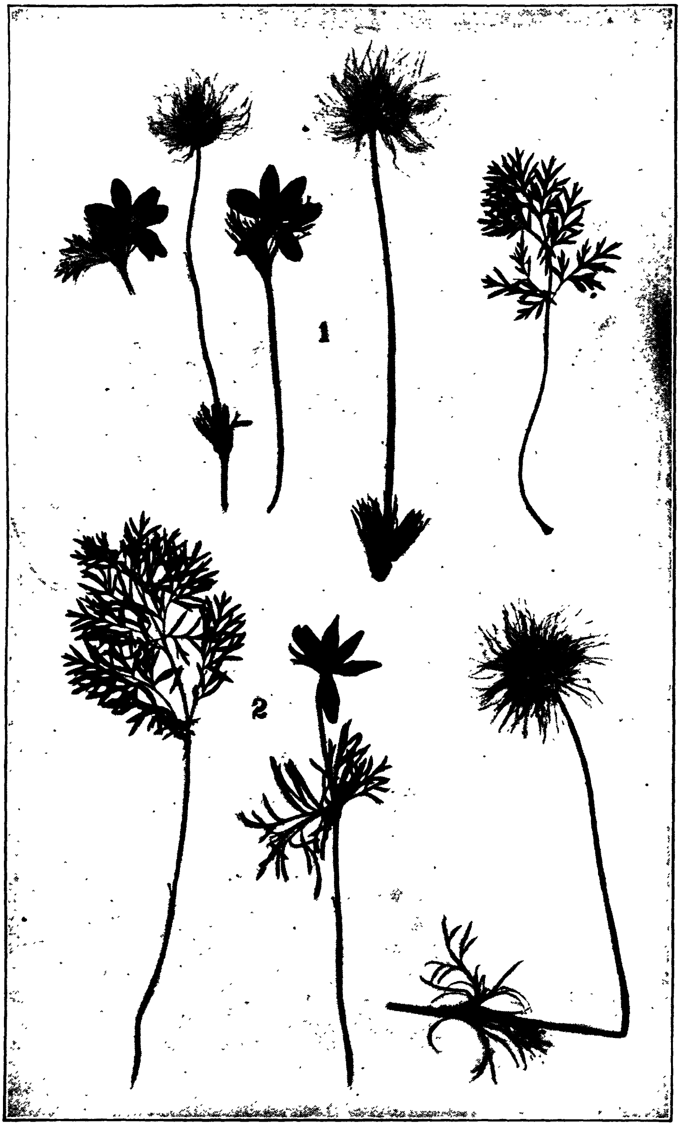


FIG. 126.—*1*, leaf, fruits and flowers of *Anemone pulsatilla*. *2*, leaf, flower and fruit of *Anemone pratensis*. The leaves are pinnately divided, the divisions being further incised or dissected.

The **tall larkspur** (*Delphinium urceolatum*) is common to the stock ranges of the Western States, and cattle grazing in these territories become poisoned by eating it. The plant is said to lose its toxic properties after it has flowered. The low larkspur has the same poisonous properties as the former.

Pulsatilla, or Pasque Flower (U. S. P. 1882 to 1905; N. F. 1916 to 1947) is the dried herb of *Anemone pulsatilla* Linné, *Anemone pratensis* Linné, or *Anemone patens* Linné. The plants are perennial herbs, *A. pulsatilla* and *A. pratensis* being indigenous to southern Europe, and *A. patens* indigenous to the western United States and Canada. Flowers appear early in the spring. The drug should be collected in the flowering stage and carefully dried. Most of the supply comes from Czechoslovakia, although some is cultivated in the western United States.

For description of the drug see Figure 126 and the National Formulary, 8th edition.

The powdered drug contains numerous simple, thick-walled hairs up to 2.5 mm. in length and 20 microns in thickness; tracheæ up to 35 microns in width with spiral thickenings, or with simple or bordered pores; fragments of epidermal tissue with broadly elliptical stomata up to 55 microns in length in leaf tissue, and up to 65 microns in length in stem tissue; calcium oxalate crystals and starch grains few or absent. The color of the powder is light olive-brown to dusky greenish yellow; the taste is very acrid.

The drug contains an acrid volatile oil, the principal constituent of which is a camphor (anemonol). The latter is easily decomposed into anemonin to which the activity of the drug is due, and which on fusion becomes exceedingly acrid. Similar principles are found in species of *Anemone*, as well as in certain species of *Ranunculus* (buttercup) and in *Clematis vitalba* of Europe.

Pulsatilla is a diuretic, an alterative, an expectorant and an emmenagogue. Average dose, 0.3 gm.

Hepatica, or Liverwort (U. S. P. 1831 to 1882) is the dried leaves of *Hepatica triloba* Chaix. The plant is a perennial, stemless herb indigenous in shady woods to Europe and North America as far south as Georgia. The leaves are subcoriaceous, smooth, dark green, broadly cordate or reniform and three-lobed. The drug may have some tonic and stimulant properties, and may be given freely in infusion.

Ranunculus, or Crowfoot (U. S. P. 1820 to 1882) is the fresh herb of *Ranunculus bulbosus* Linné, an herbaceous plant up to 45 cm. high with long-petiolate, ternate, hairy radical leaves and yellow flowers. The fresh plant is strongly acrid which decreases upon drying. It has been applied externally as a counter-irritant. It is not used internally.

Adonis, or Pheasant's Eye (N. F. 1916 to 1946) is the dried overground portion of *Adonis vernalis* Linné. The plant is fabled to have sprung from the blood of the beautiful Adonis, and the specific name indicates spring. It is a low-growing perennial herb indigenous to northern Europe and Asia. The overground portion is collected in the spring, carefully dried and tied into bundles. Most of the drug comes from plants cultivated in southern Europe.

The plant stem is cylindrical, more or less branching, sharply wrinkled with a few blackish, lanceolate leaf-scales at the base. The foliage leaves are numerous, sessile, clasping the stem, pinnately divided or pinnately compound, the ultimate divisions being linear and acute. The flowers are mostly single, terminal and about 3.5 cm. in breadth; with yellowish petals, indefinite stamens, and numerous pistils, forming in the fruit a dense head of ovoid achenes.

The powdered drug is grayish green, with a slight odor, and a slightly acrid bitter taste. It contains numerous fragments of pith parenchyma; groups of narrow sclerenchymatous fibers, mostly with lignified walls; tracheæ up to 35 microns in width, with spiral thickenings or bordered pores; leaf epidermis of finely striated cells with wavy walls and broadly elliptical, deeply embedded stomata; non-glandular hairs one-celled, somewhat curved, and occasionally in the form of double hairs; starch grains and calcium oxalate crystals very few or wanting.

The drug contains adonidin, a mixture of glucosides having the physiological action of digitalis, and of which picroadonidin is the cardiac principle; also adonidic acid and a substance resembling quercitrin; total ash about 10 per cent; acid-insoluble ash about 0.5 per cent.

Adonis is a cardiac stimulant. Average dose, 125 mg.

Herba Adonidis Æstivalis is the dried overground plant of *Adonis æstivalis*. The drug contains 0.215 per cent of a glucoside, which resembles adonidin, but is weaker in its physiological action.

In *Adonis microcarpa*, growing in Sicily, occurs a principle resembling adonidin.

Coptis, or Goldthread (U. S. P. 1820 to 1882; N. F. 1916 to 1936) is the entire plant of *Coptis trifolia*, a low perennial growing in moist woods and swamps of the northeastern United States and Canada, extending to Alaska.

Coptis occurs in loose, matted masses consisting of a nearly equal mixture of the leaves and the filiform orange-colored rhizomes, and having a slight odor and bitter taste. The leaves are radical, ternately divided, with coriaceous, obscurely three-lobed and sharply toothed leaflets. The flowers are small and whitish or light brown. For the structure see Figure 127.

An infusion prepared by placing 5 gm. of the powdered drug in 50 cc. of cold water and allowing to stand for a few minutes, with occasional stirring and then filtering, gives a golden-yellow solution.

It contains two alkaloids, berberine and coptine, the latter being crystalline and becoming purple on the addition of sulfuric acid and warming. Total ash from 3.75 to 5.25 per cent; acid-insoluble ash about 0.5 per cent.

Coptis is a tonic and a stomachic. It has an action similar to that of hydrastis. Average dose, 2 gm.

The dried rhizome of *Coptis anemonæfolia* and of several other species of *Coptis* is official in the Pharmacopœia of Japan. The rhizome is tuberculate, more or less curved, about 4 cm. in length and from 1 to 5 mm. in thickness; externally grayish yellow, bearing at the crown the remains of the leaf-bases and beset with numerous thin roots; fracture short, fibrous; inner surface with a dark orange-colored cortex, a pale yellow wood, and a large hollow pith; inodorous; taste bitter.

Zanthorrhiza, or Yellow-Root (U. S. P. 1820 to 1882) is the rhizomes and roots of *Zanthorrhiza apiifolia*. The plant is shrubby, up to 60 cm. high, growing in eastern United States from New York to Mexico. The rhizome is much-branched and bent, long and up to 15 mm. thick, yellowish brown and with few rootlets. The bark is thin, deep yellow; the wood striate, bright yellow. The powdered drug is very bitter and starchy. The drug contains berberine and probably a colorless alkaloid. It is a tonic and alterative. Dose, 2 gm.

Black Hellebore (U. S. P. 1820 to 1882) is the rhizome and roots of the Christmas or New Year's Rose, *Helleborus niger*, a perennial herb indigenous to the forests of the eastern and southern Alps and also cultivated. It produces pinkish flowers during the winter, or very early in the spring, long before any other plant flowers.

The rhizome is horizontal, with numerous short, knotty branches and moderately long roots; externally grayish black or brownish black, upper surface with numerous stem-bases and depressed circular scars, under and side portions with numerous root-bases; fracture short and mealy; internally light yellow, showing a number of broad wood wedges; odor distinct; taste bitter.

Roots from 2 to 3 mm. in thickness, yellowish or dark brown, with a thick light brown cortex and a narrow, central, porous, yellowish wood.

It contains two crystalline glucosides: helleborin, a narcotic poison with burning taste, and helleborein, a cardiac stimulant having a sweetish taste. The former gives a violet-red color with concentrated sulfuric acid, and the latter a deep violet color with the same reagent. The drug also contains a volatile oil, two acrid resins, an acrid fixed oil, aconitic acid and gallates of calcium and potassium.

Black hellebore is a heart stimulant, a drastic hydragogue cathartic and an emmenagogue.

It is used somewhat in veterinary practice but its use in medicine is obsolete.

Black hellebore has appeared on the market under the label of "American Hellebore" (see page 150).

Helleborus Fœtidus, or Bear's-foot Hellebore (U. S. P. 1820 to 1831) is the leaves of *Helleborus fœtidus*, an English species, often cultivated for its flowers. Now, rarely used in medicine.

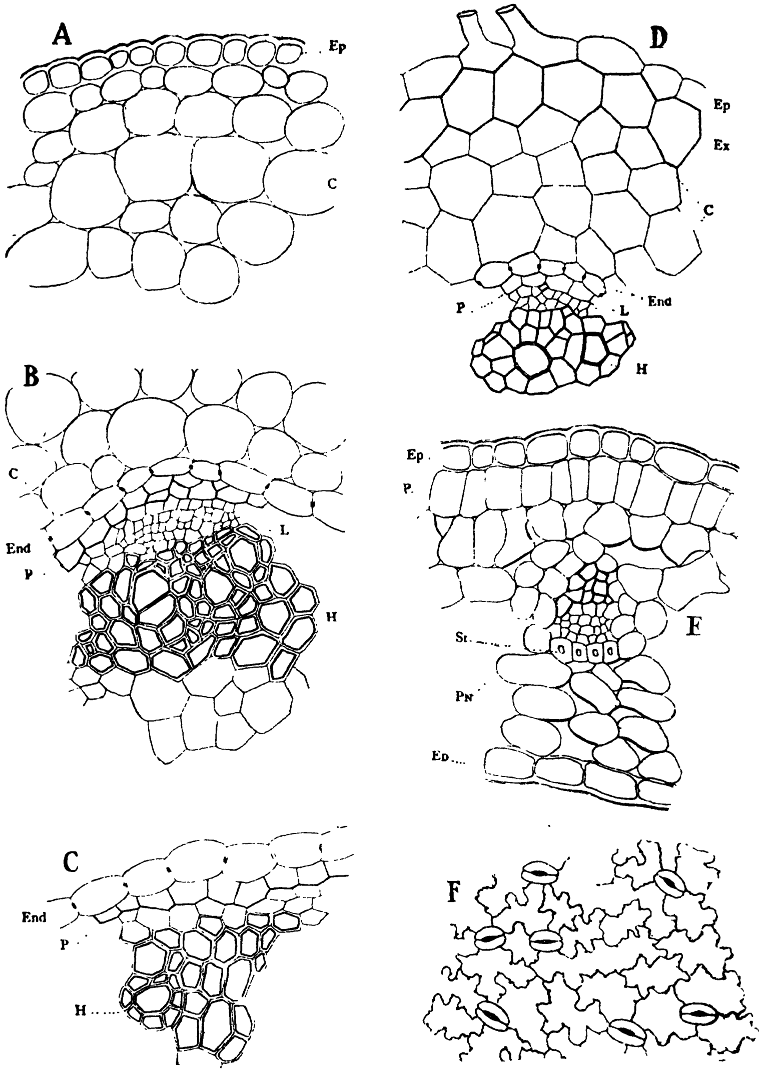


Fig. 127.—Coptis: *A*, transverse section of peripheral portion of an internode in the rhizome: *Ep*, epidermis; *C*, cortex. *B*, transverse section of rhizome: *C*, cortex; *End*, endodermis; *P*, pericycle; *L*, phloem; *H*, the xylem or vessels. *C*, section of same internode as in *A* and *B* showing the wood fibers (*H*) between the two arches of collateral mestome bundles. *D*, transverse section of a root: *Ep*, epidermis; *Ex*, exodermis; *C*, cortex; *End*, endodermis; *P*, pericycle; *L*, phloem; *H*, xylem. *E*, transverse section of a leaflet: *Ep*, the epidermal cells of the ventral surface; *Ed*, epidermal cells of the lower or dorsal surface; *P*, palisade cells; *Pn*, loose mesophyll tissue; *St*, stone cells on the phloem side of a lateral vein. *F*, surface view of the dorsal or lower epidermis of a leaflet showing the stomata and foldings of lateral cell walls. (After Holm.)

BERBERIDACEÆ, OR BARBERRY FAMILY

This is a small family of about 100 species of herbs and shrubs, growing mostly in temperate regions. The flowers are either single or in racemes and the fruit is a berry or capsule. A number of crystalline substances are present and some of these, as berberine, are very characteristic of the plants of this family. The non-glandular hairs are usually unicellular; in some instances they consist of a chain of cells, the terminal one of which is filled with a yellowish or brownish amorphous substance.

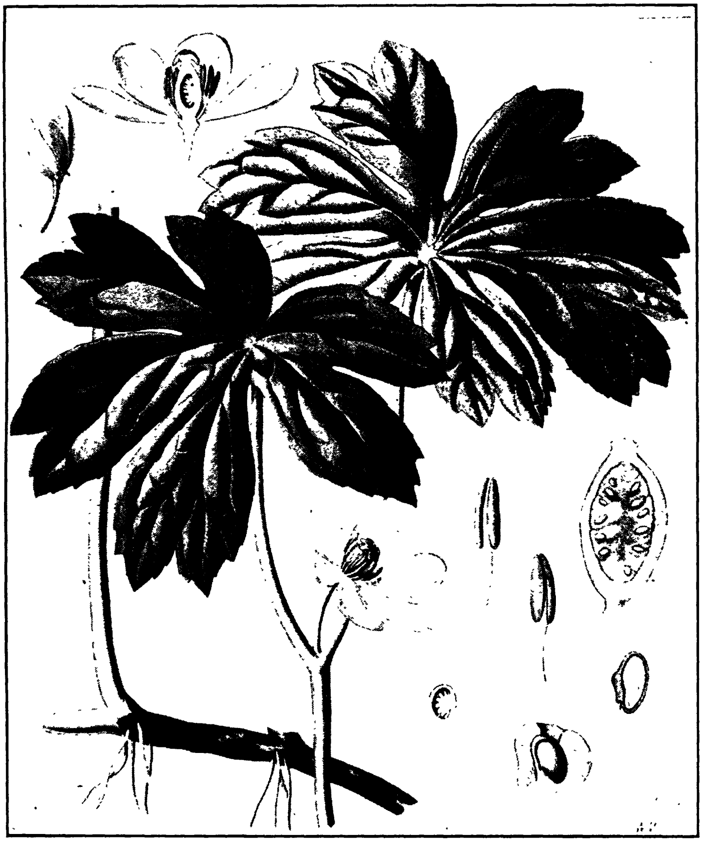


FIG. 128.—*Podophyllum peltatum:* A portion of the long, horizontal, branched, nearly cylindrical, dark brown rhizome, with internodes 2 to 10 cm. in length, and roots from the underside of the nodes and a stem-scar, aërial stem or bud from the upper side; the two large, peltate, deeply lobed leaves arising from the top of the stem with the large, white-petaled flower between them; the bud and the flower in median longitudinal section (upper left corner); the stamens, the ovary in cross-section, the fruit in longitudinal section, the ovule and the seed in longitudinal section (lower right corner). (After Köhler.)

PODOPHYLLUM

Podophyllum, Mandrake or May Apple (U. S. P. 1820 to 1942; N. F. 1942 to date) consists of the dried rhizome and roots of *Podophyllum peltatum* Linné.

The generic name is from the Greek and means foot-like leaf; *peltatum* means shield-like. The plant is a perennial herb having a long jointed and branching rhizome. The rhizomes are dug either early in the spring or in the autumn, after the aërial parts have died down. Most of the commercial supplies come from the Central States and from

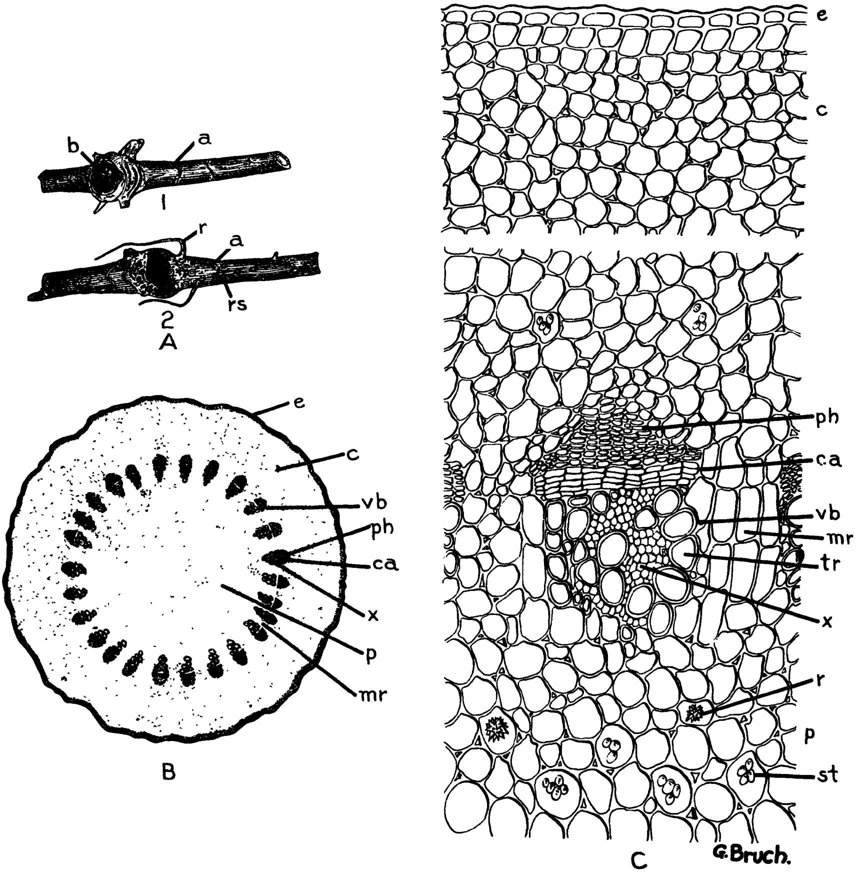


FIG. 129.—*Podophyllum peltatum: A*, entire drug showing the nearly cylindrical, jointed rhizome somewhat compressed on the upper and lower surfaces; up to 9 mm. in diameter (internodes), with thickened nodes; dark brown; longitudinally wrinkled with irregular V-shaped scars (*a*) of the scale leaves. The upper view (*1*) shows a large circular depressed stem-scar (*b*); the lower view shows numerous root-scars (*rs*) or roots (*r*) about 2 mm. in thickness. The fracture is short, the odor slight and the taste disagreeably bitter and acrid. *B*, lens view of a transverse section through the internode of the rhizome showing epidermis (*e*); cortex (*c*); vascular bundles (*vb*), containing phloem (*ph*) and xylem (*x*) separated by cambium (*ca*); medullary rays (*mr*) and pith (*p*). *C*, transverse section from the periphery into the pith with a portion of the cortex omitted, showing epidermis (*e*) with outer and radial walls suberized; cortex (*c*) of parenchyma cells; open collateral vascular bundles (*vb*); phloem (*ph*); xylem (*x*), containing tracheæ (*tr*); cambium (*ca*); and pith (*p*). The cells of the cortex and pith contain single or 2- to 6-compound starch grains (*st*) from 3 to 20 microns in diameter and rosette aggregates of calcium oxalate up to 80 microns across. (Drawing by G. Bruch.)

Virginia and North Carolina. The drug was long known to the Indians, who introduced it to the early settlers.

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 128 and 129 and the National Formulary.

CONSTITUENTS.—Resin 3.5 to 5 per cent, consisting of two poisonous principles: (*a*) podophyllotoxin occurring in white crystals that are insoluble in water, and (*b*) picropodophyllin (an isomer of podophyllotoxin) which crystallizes in needles and is insoluble in water but soluble in 95 per cent alcohol. Podophyllotoxin, on treatment with dilute alkali solutions, takes up a molecule of water and forms a gelatinous unstable acid (podophyllic acid). This acid by loss of water forms crystalline picropodophyllin. The resin also contains a yellow, crystalline flavinol, quercetin, a green fixed oil, podophyllic acid, a purgative resin, podophylloresin; considerable starch, and some gallic acid. Total ash 3.25 per cent; acid-insoluble ash 0.4 per cent.

STANDARDS.—Podophyllum yields not less than 5 per cent of resin of podophyllum and contains not more than 3 per cent of foreign organic matter.

USES AND DOSE.—Podophyllum is a drastic purgative or hydragogue cathartic. It has also been used as a skin irritant. Average dose, 0.2 gm.

ALLIED PLANTS.—**Podophyllum Indicum, B. P.**, the rhizome of *Podophyllum emodi*, a plant growing on the lower slopes of the Himalayas, is larger and yields 11.4 to 12 per cent of resin, which contains about twice as much podophyllotoxin as the resin obtained from *P. peltatum.*

Podophyllum Resin (U. S. P. 1863 to 1942; N. F. 1942 to date) is prepared by extracting finely powdered podophyllum by slow percolation with alcohol, concentrating the alcoholic extract, and pouring it into acidified water. The precipitated resin is washed twice with water, dried and powdered. It is an amorphous powder varying in color from light brown to greenish yellow and turns darker when subjected to temperatures exceeding 25° C. It has a slight, peculiar, bitter taste and is very irritating to the eye and to mucous membranes. Podophyllum resin is soluble in alcohol with only a slight opalescence, and the solution is acid to litmus. It is only partially soluble in ether and in chloroform.

TESTS.—It is soluble in potassium or sodium hydroxide solutions, forming a deep yellow liquid from which it may be precipitated with acids. When a hot aqueous solution is allowed to cool, it deposits most of its contents, and if this cool solution is filtered, the filtrate has a bitter taste and turns brown upon the addition of a drop of ferric chloride T.S.

Add 0.4 gm. of podophyllum resin to 3 cc. of 60 per cent alcohol, follow with 0.5 cc. of potassium hydroxide T.S., and shake the mixture gently; it does not gelatinize (difference from *Podophyllum emodi* resin).

USES AND DOSE.—Podophyllum resin is a drastic purgative and hydragogue cathartic. Average dose, 10 mg.

Berberis, Oregon Grape Root or Berberis Aquifolium (U. S. P. 1905 to 1916; N. F. 1916 to 1947) consists of the dried rhizome and roots of species of the section *Mahonia* (Nuttall) DeCondolle of the genus *Berberis* Linné. The plants are low trailing shrubs indigenous to the Rocky Mountain region extending into British Columbia and as far east as Nebraska. Most of the commercial supplies are gathered in Washington, Oregon and California, chiefly from *Mahonia aquifolium.* Berberis was introduced into American medicine in 1877 by Bundy. The East Indian varieties of *Berberis* were used in medicine by Dioscorides, Pliny and Galen.

See Figures 130, 131 and National Formulary, Edition 1942, for the description, structure and powder.

Berberis contains four alkaloids: namely, berberine; oxyacanthine, which acquires a yellow color in sunlight; berbamine, which is distinguished by being soluble in water; and another alkaloid whose properties have not been investigated. The drug also contains resins and considerable starch. Total ash about 1.83 per cent; acid-insoluble ash about 0.33 per cent.

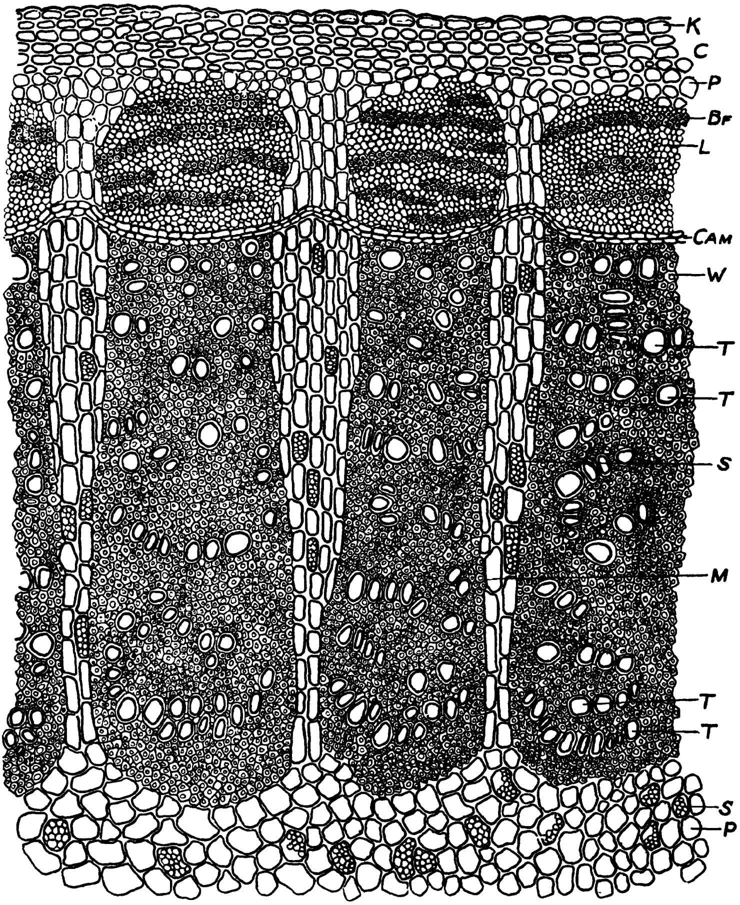


Fig. 130.—Transverse section of Berberis rhizome consisting of a few layers of cork (*K*), a narrow cortex (*C*) of parenchyma (*P*), containing yellowish brown amorphous contents. Numerous open collateral fibrovascular bundles separated by medullary rays (*M*) containing starch (*S*). Each bundle consists of an outer phloem consisting of alternating rows of bast fibers (*BF*) and leptome (*L*); a narrow cambium and a broad xylem consisting of numerous wood fibers (*W*) intermingled with pitted and reticulate tracheæ (*T*). A narrow central pith composed of parenchyma (*P*) containing starch (*S*). Sections of the root are similar to those of the rhizome except that they exhibit curved medullary rays and show no pith. (Drawing by Haase.)

Berberis contains not more than 5 per cent of attached overground stems and not more than 2 per cent of other foreign organic matter, and yields not more than 2 per cent of acid-insoluble ash. Pieces of the rhizome or root over 45 mm. in diameter or pieces from which the bark has been removed must be rejected.

Berberis is a bitter tonic and an alterative. Average dose, 2 gm.

Berberis Baccæ (U. S. P. 1831 to 1842, N. Y. Edition), the fresh fruit of *Berberis canadensis* Mill (American Barberry) has been used in an acidulous drink as a febrifuge.

Berberis, or Barberry Bark (U. S. P. 1863 to 1882), the bark of the root of *Berberis vulgaris* Linné (European Barberry), naturalized in the eastern United States, is a drug with properties similar to those of the Oregon Grape.

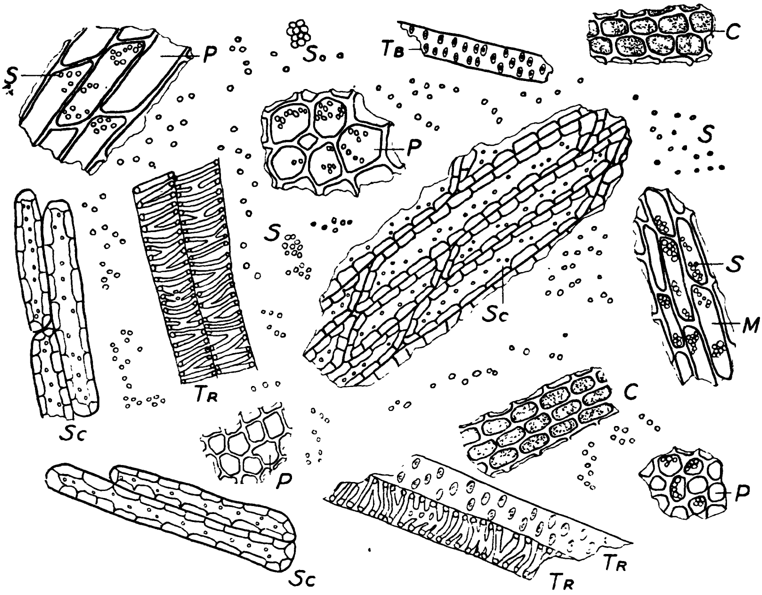


FIG. 131.—Powdered Berberis or Oregon Grape.—Yellowish brown; consisting of fragments of medullary rays (*M*), containing starch grains (*S*) (2- to 3-compound, the individual grains from 3 to 20 microns in diameter); reticulate tracheæ (*TR*) and tracheæ with bordered pores (*TB*); wood and bast fibers (*SC*); fragments of cortical parenchyma (*C*), containing a yellowish brown amorphous substance and fragments of parenchyma from the pith (*P*). (Drawing by Haase.)

Not only the rhizomes and roots, but also the stem and root barks are employed, the root bark containing a larger amount of alkaloids than that of the stem.

The bark and root of *Berberis asiatica* of the Himalaya region and *B. aristata* of India are similarly employed, the latter containing about 2 per cent of berberine.

The flowers and berries of *Mahonia aquifolium* and *B. vulgaris* contain berberine, oxyacanthine, volatile oil, about 6 per cent of malic acid and 3.5 to 4.7 per cent of sugar.

The alkaloid berberine is also found in *Argemone mexicana* (Fam. *Papaveraceæ*) and in the following members of the *Ranunculaceæ: Hydrastis canadensis, Coptis trifolia,* and *Zanthorhiza apiifolia.*

CAULOPHYLLUM

Caulophyllum or Blue Cohosh (U. S. P. 1882 to 1905; N. F. 1916 to date) consists of the dried rhizome and roots of *Caulophyllum thalic-*

troides (Linné) Michaux. The generic name is from two Greek words meaning a stem-leaf, in reference to the overground characteristic of the plant; *thalictroides* means "like meadow rue" and is also of Greek origin.

The plant is a perennial herb having a more or less crooked horizontal rhizome. It is indigenous to the eastern part of the United States and Canada. Caulophyllum was used by the American Indians as a parturient.

Description.—The rhizome is horizontal, with a few upright branches, from 7 to 25 cm. in length and from 5 to 15 mm. in thickness; externally grayish brown to dark reddish brown, the upper surface with numerous depressed cup-shaped scars or short stem-bases; under and lateral portions with numerous grayish brown or yellowish brown, matted branching roots; the fracture of the rhizome is rough and woody and of the roots tough; the rhizome has, when smoothly cut, a waxy luster and shows a thin bark, numerous small wood wedges and a large pith. The root consists of a thick cortex of starch-bearing parenchyma, and a 4-rayed xylem.

Powder.—Pale to yellowish brown, odorless but sternutatory and with an acrid and bitter taste; the powder shows numerous starch grains from 3 to 18 microns in diameter, mostly simple, somewhat spheroidal in shape; fragments of cork having yellowish brown walls; tracheæ from 25 to 50 microns in width, with bordered pores; sclerenchymatous fibers with strongly lignified walls; tracheids with bordered pores; and fragments of starch-bearing parenchyma.

Constituents.—A crystalline alkaloid, methylcytisine (caulophylline); a crystalline glucoside, caulosaponin (leontin); a second saponin-like glucoside, caulophyllosaponin; a phytosterol glucoside, to which the name citrullol has been applied; a phytosterol; and a mixture of fatty acids. Total ash 3.3 per cent; acid-insoluble ash 0.5 per cent.

Standards.—Caulophyllum contains not more than 3 per cent of foreign organic matter and yields not more than 4 per cent of acid-insoluble ash.

Uses and Dose.—Caulophyllum is said to be an antispasmodic, an emmenagogue and a diuretic. Average dose, 0.5 gm.

MENISPERMACEÆ, OR MOONSEED FAMILY

This family, comprising about 300 genera, consists mostly of tropical plants which are in the nature of climbing or twining, frequently woody, vines. The leaves are entire or lobed, the flowers are small, white or green, and diœcious. The stems are characterized by having broad primary medullary rays, and in the pericycle there is usually a continuous sclerenchymatous ring. The tracheæ are porous, very wide and are associated with tracheid-like wood fibers. In certain of the genera in which the stem is thick and woody an anomalous structure is found, consisting of several rings of vascular bundles, which rings are concentric or may develop eccentrally; that is, more strongly on one side, as in Pareira. Calcium oxalate usually occurs and both glandular and non-glandular hairs may be present; peculiar hydathodes, *i. e.*, water-absorbing and water-excreting organs, are observed situated among the trichomes in *Anamirta cocculus*. Elongated secretory sacs occur in the stems and petioles of *Cissampelos, Jateorrhiza* and *Anamirta.* A sub-epidermal mucilaginous layer occurs in a number of species.

CALUMBA

Calumba or Colombo (U. S. P. 1820 to 1936; N. F. 1936 to date) is the dried root of *Jateorrhiza palmata* (Lamarck) Miers. The generic name is derived from two Greek words, meaning a healing root. *Palmata* refers to the leaves which are palmately lobed. The name calumba is derived from *kalumb,* the native African name for the root.

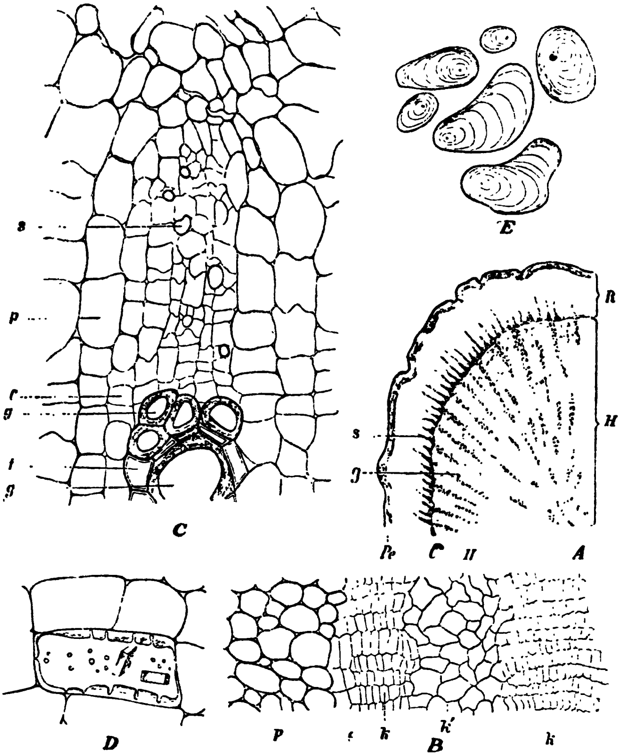


Fig. 132.—Calumba: *A*, transverse section showing bark (*R*), cambium (*C*) and wood (*H*), wood fibers (*H*), tracheæ (*g*), periderm (*Pe*) and phloem (*s*); *B*, transverse section of periderm showing parenchyma (*p*), small-celled cork (*k*) and large-celled cork (*k'*); *C*, transverse section near cambium showing tracheæ (*g*, *g*), intermediate fiber (*i*), cambium (*c*), parenchyma (*p*) and sieve cell (*s*); *D*, stone cell from the periderm containing calcium oxalate; *E*, lamellated starch grains. (After Meyer.)

The plant is a perennial woody climber indigenous to Mozambique and Madagascar. The roots are dug in the dry season (March), separated from the rhizomes, cut into transverse or oblique slices, and dried in the shade. Calumba seems to have come into general use during the latter part of the eighteenth century.

Description.—In nearly circular or elliptical disks, sometimes irregularly bent, up to 10 cm. in diameter and 20 mm. in thickness; the bark is 4 to 6 mm. in thickness with a distinct cambium zone; externally pale reddish brown to light olive-brown and coarsely wrinkled; fracture short, mealy; the cut surface is yellowish and radiate, the collateral bundles forming a concentric zone; center usually depressed.

STRUCTURE.—See Figure 132 and the National Formulary.

POWDER.—Greenish yellow; odor slight; taste slightly aromatic, very bitter; starch grains numerous, mostly simple, from 3 to 85 microns in length, ovoid, ellipsoidal, frequently very irregular, slightly lamellated, with eccentral, linear, X-shaped or branching clefts; stone cells few, having irregularly thickened, strongly lignified, coarsely porous walls and often containing one or more prisms of calcium oxalate from 10 to 30 microns in length or numerous small, spheroidal microcrystals; fragments with tracheæ few, the latter with reticulate thickenings, or bordered pores, and associated with wood fibers having long, oblique, slit-like pores.

CONSTITUENTS.—Several yellowish alkaloids, closely resembling berberine and varying from 0.98 to 1.38 per cent in the bark and 1.02 to 2.05 per cent in the wood. To some of these bases the names columbamine, palmatine and jateorrhizine have been given. Calumba also contains a volatile oil, 0.056 per cent; starch, about 35 per cent; pectin, 17 per cent; resin, 5 per cent; calumbic acid; calcium oxalate, and mucilage. Total ash, 6.32 per cent; acid-insoluble ash, 0.49 per cent.

STANDARDS.—Calumba contains not more than 1 per cent of foreign organic matter, and yields not more than 2.5 per cent of acid-insoluble ash.

USES AND DOSE.—Calumba is a bitter tonic. Since it contains no tannin, it may be prescribed with iron salts, and does not cause constipation. Average dose, 1 gm.

ADULTERANTS AND SUBSTITUTES.—Calumba is rarely adulterated, although the following have been found either as admixtures or sold under the name of calumba:

1. **Calumba rhizome,** in distinctly radiate disks up to 3 cm. in diameter, without depressed centers.
2. **Ceylon Calumba,** the stem of *Coscinium fenestratum,* occasionally found in dark yellow slices which show distinct medullary rays and crescent-shaped bands of sclerenchyma outside of the phloem patches. It is very woody and the center is not depressed.
3. **American Calumba,** the bitter root of *Frasera carolinensis* Fam. *Gentianaceæ* occurs in transverse disks somewhat resembling calumba, but without radiate structure.
4. The roots of *Tinospora bakis,* a tropical African plant, have also been found in the market.

Menispermum, or Canada Moonseed (U. S. P. 1831 to 1842, N. Y. edition, 1882 to 1905) is the dried rhizom of *Menispermum canadense.* This plant is a high-climbing vine, indigenous to the northern United States and Canada and having broadly ovate, cordate and 3- to 7-lobed leaves. The long slender rhizome, cut into convenient pieces and dried, is horizontal, cylindrical, much branched, and attains a diameter of 20 mm.; it is yellowish to dark brown, longitudinally wrinkled and somewhat scaly, having nodes, buds, circular overground stem-scars and scattered roots; fracture tough and very fibrous; the rhizome has a thin bark, a broad porous radiating wood, and a white pith which is frequently hollow in the larger pieces; inodorous; taste bitter and somewhat sweetish. Roots cylindrical, more or less branching, from 0.5 to 2 mm. in diameter, dark brown, tough, wiry. The structure is shown in Figure 133.

Menispermum contains the bitter alkaloid menispine, berberine, oxyacanthine and starch. It is used as a tonic, an alterative, and a diuretic.

Pareira (U. S. P. 1842 to 1916; N. F. 1916 to 1936) is the root of *Chondrodendron tomentosum,* a perennial climber indigenous to Brazil and Peru. The commercial article (see Fig. 134) is exported from Rio Janeiro, is nearly cylindrical, more or less tortuous, cut into pieces up to 20 cm. in length, and varying from 1 to 6 cm. in diameter; externally brownish black with transverse ridges

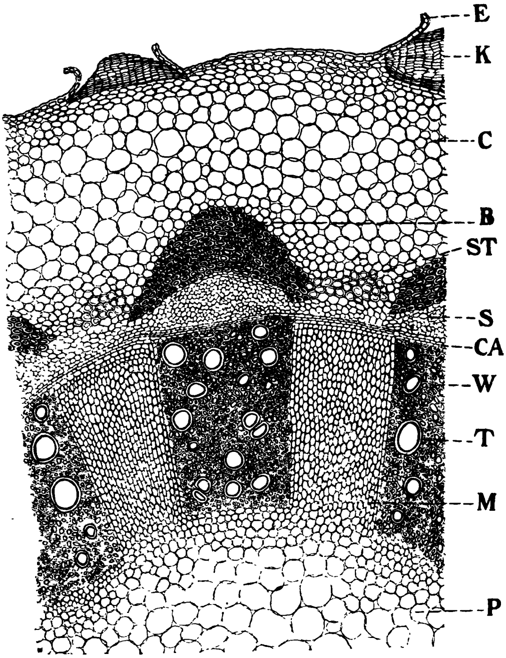


FIG. 133.—Menispermum. Transverse section through rhizome: *E*, epidermis; *K*, subepidermal cork; *C*, cortex; *B*, bast fibers; *S*, sieve; *ST*, stone cells; *CA*, cambium; *T*, large tracheæ or vessels; *W*, wood fibers; *M*, medullary ray cells; *P*, pith.

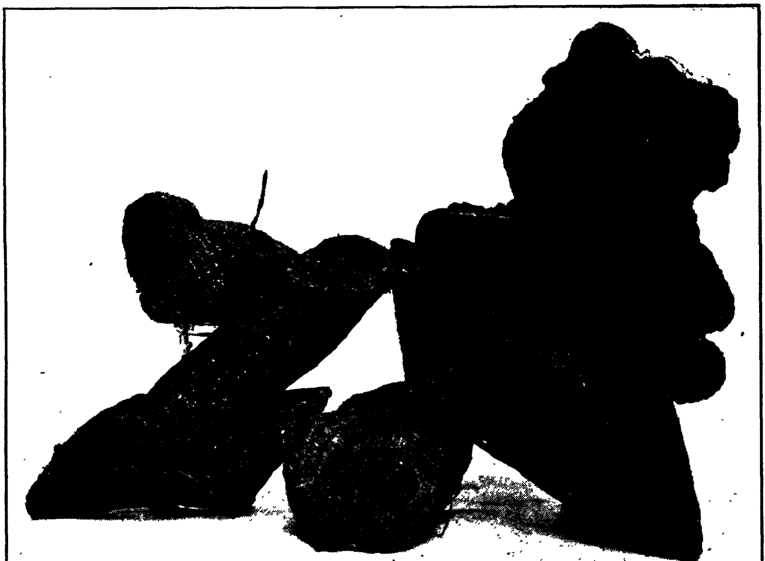


FIG. 134.—Photographs of typical specimens of true Pareira, the pieces in transverse section showing concentric rings of fibrovascular tissue.

and knot-like projections, occasional fissures, and longitudinal wrinkles or even furrows; hard, heavy and tough; when freshly cut having a waxy luster; the transverse surfaces exhibiting several successive eccentral and distinctly radiate concentric zones of projecting secondary fibrovascular bundles, each 2 to 4 mm. wide, the zones separated by distinct concentric zones of parenchyma and stone cells; odor slight; taste very bitter.

Pareira contains several alkaloids, bebeerine (pelosine), isobebeerine, β-chondrodendrine, β-bebeerine, and chondrodine. A mixture of the sulfates of these alkaloids constitutes the commercial bebeerine sulfate.

Pareira is used as a bitter tonic, an antipyretic, and a diuretic. Average dose, of the drug, 2 to 4 gm.; of bebeerine sulfate as a tonic, 30 to 100 mg., as an antipyretic, 0.2 to 1 gm.

ALLIED PLANTS.—**White Pareira** is obtained from *Abuta rufescens*, the roots of which are whitish or pale yellow and very starchy. **Yellow Pareira** is obtained from *A. amara.* The root is bright yellow internally, very bitter, and apparently contains alkaloids resembling bebeerine and berberine. **False Pareira** is obtained from a related species (*Cissampelos pareira*), growing in South America, the West Indies and the East Indies. The root is somewhat flattened, externally dark brown, internally yellowish brown, free from the concentric zones of wood bundles, and contains about 0.5 per cent of pelosine.

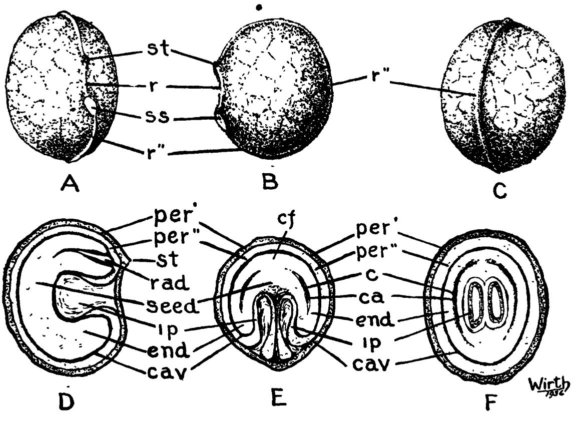


FIG. 135.—Cocculus. Fruits spheroidal, ovate or subreniform, 8 to 13.5 mm. long, 7 to 11 mm. wide and 7 to 10 mm. thick, wrinkled, blackish brown or reddish brown. *A*, ventral view; *B*, side view; *C*, dorsal view, showing stalk-scar (*ss*) and a slight protuberance (*st*) (the remains of the stigma) connected by a short ridge (*r'*) on the ventral side. A longer and more or less obscure ridge (*r''*) extends around the dorsal side of the fruit. *D*, vertical section of the fruit cut along the ridge; *E*, transverse section; *F*, vertical section cut at right angles to the ridge plane, showing the outer brownish layer (*per'*) and the inner yellowish layer (*per''*) of the pericarp (about 1 mm. thick); the reniform seed (*seed*) and the ventral infolding of the pericarp (*ip*). The embryo consists of thin cotyledons (*e*) embedded in longitudinal cavities (*ca*) in the endosperm (*end*). The radicle (*rad*) is visible in the vertical section. *Cav*, cavi-endosperm (*end*). The radicle (*rad*) is visible in the vertical section. *Cav*, cavities due to shrinkage; *cf*, fat crystals in the endosperm (Drawings by Wirth.)

Nectandra, or Bebeeru Bark (U. S. P. 1863 to 1882) is the dry bark of *Nectandra Rodiæi* (Fam. *Lauraceæ*), the greenheart tree, 60 to 100 feet high, growing on hillsides in British Guiana near the sea. The wood is very durable. The bark is in flat, brown pieces about 6 mm. thick. It is astringent and very bitter in taste. It contains the alkaloid bebeerine (pelosine) and the bark has been used for the production of this alkaloid or mixture of alkaloids.

The wood of the **boxwood** (*Buxus sempervirens*, Fam. *Sapindaceæ*) contains an alkaloid, buxine, resembling bebeerine.

Cocculus, or Cocculus Indicus (N. F. 1916 to 1947) is the dried ripe fruit of *Anamirta cocculus* (Linné) Wight et Arnott.

The plant is a woody climber growing in the mountainous woods of southeastern Asia, particularly along the Malabar coast. The fruits are commonly used by the natives to stupefy fish, thus making it possible to catch them by hand. When ripe they are of a reddish color and are removed from their stalks and dried. The drug seems to deteriorate with age, and those fruits which are of a dark color, having the seeds well preserved, are preferred.

DESCRIPTION AND STRUCTURE.—See Figure 135.

POWDER.—Moderate yellowish brown; odorless; taste bitter, the seed intensely bitter; numerous fragments of epicarp becoming reddish brown upon the addition of alkalis; fragments of endosperm parenchyma, the cells containing aleurone grains up to 50 microns in length, many fixed oil globules, and acicular crystals, the latter soluble in diluted hydrochloric acid and insoluble in water, alcohol or potassium hydroxide T.S.; numerous thick-walled, mostly non-lignified fibers; tracheæ spiral.

CONSTITUENTS.—Picrotoxin 1.5 per cent; fixed oil up to 25 per cent, consisting chiefly of stearic and oleic acids; the pericarp contains two tasteless, non-toxic, crystallizable alkaloids, vis menispermine and para-menispermine. Total ash, about 5.5 per cent; acid-insoluble ash, about 0.15 per cent.

Cocculus is a convulsant poison and the tincture is used as a parasiticide.

Picrotoxin, or Cocculin (U. S. P. 1882 to 1905, 1942 to date) is a glycoside obtained from the seed of *Anamirta paniculata* Colebrooke.

It is an equimolecular compound of picrotin and picrotoxinin, and forms colorless, odorless, shining prismatic crystals, stable in air, but affected by light. It is readily soluble in cold or boiling alcohol, boiling water and diluted acids and alkalis, but sparingly soluble in ether, in chloroform and in water. It melts at 198° to 200° C.

Picrotoxin has been used as an antihidrotic, and as an antidote in barbiturate poisoning; also in ointments as a parasiticide, but it is considered dangerous. It is very poisonous. Dose, subcutaneous, 2 mg.

MAGNOLIACEÆ, OR MAGNOLIA FAMILY

The plants of this family are mostly trees or shrubs and are represented in the United States by the magnolias and the tulip tree which is also called yellow poplar or white wood. The plants are characterized by having in the pericycle small isolated groups of bast fibers. The pith is frequently hollow, surrounded by more or less empty cells, those at the periphery being thick-walled and living. The stone cells are of various shapes, being not infrequently much branched, as in magnolia. Calcium oxalate occurs in the form of small octahedral or prismatic crystals or in rosette aggregates, seldom in the form of large prisms. An important character is the presence of more or less spheroidal secretory cells which are distributed in the parenchyma of the stem and leaves, and contain either a volatile oil or resin. In the leaves they give rise to pellucid dots, which are apparent on holding the leaves to the light.

Magnolia (U. S. P. 1820 to 1894) is the dried bark of *Magnolia virginiana* Linné (*M. glauca* or Sweet Bay) or of other species of *Magnolia*. The bark from the younger branches of the Sweet Bay is warm and spicy, somewhat astringent and bitter in taste. The bark from older trees and from other species inclines to be thicker, darker in color, more fibrous, less aromatic. The bitterness and pungency appear to be due to a colorless crystalline principle similar to liriodendrin.

The bark has been used as a bitter tonic, antimalarial and diaphoretic. The dose is about 2 gm. in tincture or decoction.

Illicium, Chinese Anise or Star Anise (U. S. P. 1882 to 1905) is the dried, ripe fruit of *Illicium verum* Hook. f. (not *Illicium anisatum* L.), a tree indigenous to southeastern Asia and now extensively cultivated in southern China, French Indo-China, Japan, the Philippines and Jamaica.

The commercial supplies are mostly from Tonkin and are used for the distillation of the volatile oil, which closely resembles anise oil and is recognized by most of the pharmacopœias as such. The carpels of the flower are erect, assuming a horizontal position after fertilization, and the fruit is collected usually when the first follicles are well dehisced.

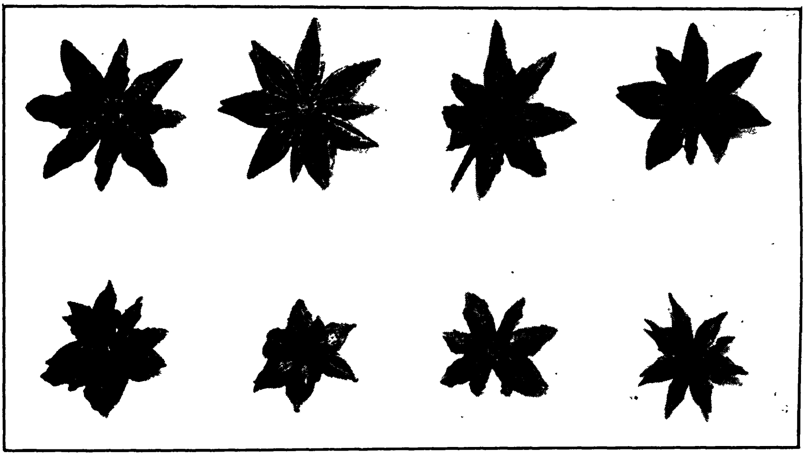


FIG. 136.—Chinese star anise (above) and Japanese star anise (below). (Photo by R. S. Adamson.)

The fruit (see Fig. 136) consists of 6 to 11 (usually 8) outspreading boat-shaped follicles, arranged around a central axis, each carpel containing a single, shiny brown seed. The fruit is brown in color, externally rough, but on the inner surface lighter in color, smooth and shiny; the odor and taste are aromatic, resembling anise. Star anise contains rather numerous irregularly branched stone cells (see Fig. 137), while in the poisonous Japanese star anise such branched cells are absent.

Illicium yields a volatile oil (see page 462) consisting chiefly of anethol, 5 to 6 per cent from the pericarp and 1.7 to 2.7 per cent from the seed. The drug also contains a reddish brown resin, fixed oil (in the seed), anisic acid, protocatechuic acid and shikimminic acid. Ash about 3 per cent.

Illicium is used as a stimulant carminative. Average dose, 1 gm.; of the volatile oil, 0.1 cc.

Japanese Star Anise, Shikimmi or Skimmi, the fruit (see Fig. 136) of *Illicium religiosum* (also known as *I. japonicum* and *I. anisatum*), is very poisonous, and is obtained from trees which are extensively cultivated in Japan, especially in groves of Buddhist temples. The fruits may be dangerous because of their resemblance to Chinese star anise, but the two kinds are seldom mixed. The carpels (see Fig. 136) are somewhat smaller than illicium, the summit being acuminate and terminated by a short curved beak. Their odor is different from anise and resembles oil of sassafras or laurel. The taste is intensely pungent, becoming aromatic, somewhat bitter and camphor-like.

The Japanese star anise yields 1 per cent of a volatile oil; and skimmin, which forms large crystals that are soluble in alcohol, but insoluble in water, and to which the poisonous properties are due. An alcoholic solution of the carpels, upon evaporation, yields numerous crystals of shikimminic acid.

Liriodendron, or Tulip-tree Bark (U. S. P. 1820 to 1882) is the bark of *Liriodendron Tulipifera* Linné. The plant is a stately tree rising to 140 feet and indigenous to the eastern United States from Vermont and Michigan to eastern Kansas and the Gulf of Mexico.

The bark is frequently freed from its cork and then is light colored, fibrous, pungently aromatic and bitter. The bitter, pungent glycoside liriodendrin gives the activity to the bark which has been used as a bitter tonic, antiperiodic and diuretic. The dose is 4 gm. in tincture or infusion.

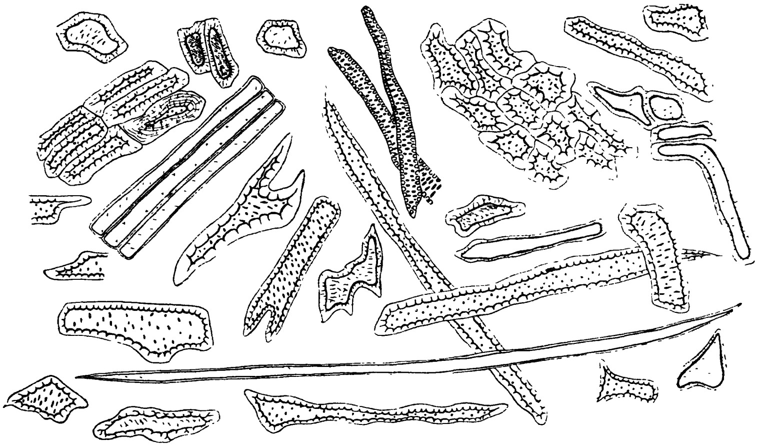


FIG. 137.—Various forms of stone cells in star anise, the fruit of *Illicium verum*.

Wintera, or Winter's Bark (U. S. P. 1820 to 1863) is the bark of *Drimys Winteri* Forster. The plant is a small tree found in western South America. The bark is rather thin, inclined to quill, mostly light gray on the outer surface and brown on the inner surface. The odor is distinctive, aromatic and the taste aromatic and pungent. The bark contains a volatile oil and about 10 per cent of a soft pungent resin. It is used as a tonic and stomachic. Dose, 2 gm.

MYRISTICACEÆ, OR NUTMEG FAMILY

This is a small family, consisting of about 80 species of tropical trees and shrubs. The leaves are entire and evergreen, the flowers are small, and the plants are diœcious. The fruit is a fleshy capsule and the seeds are covered by a fleshy arillus. Spheroidal secretion cells with suberized walls and containing a semifluid or crystalline oily substance, which is variously colored from yellow or red to brownish black, are distributed in all parts of the plant. Calcium oxalate occurs in the form of small needle-shaped crystals, which frequently are arranged in aggregates. The hairs are of stellate type and are very characteristic for several of the species.

MYRISTICA

Myristica or Nutmeg (U. S. P. 1820 to date) is the dried ripe seed of *Myristica fragrans* Houttuyn, deprived of its seed coat and arillode and with or without a thin coating of lime. The tree is indigenous to the Molucca and neighboring islands, and is now extensively cultivated in other tropical regions, including the West Indies. The botanical name *Myristica fragrans,* refers to the fragrance of the nutmeg. The commercial supply is largely derived from the Malay Archipelago, particularly the Banda Islands, and the Grenadine Islands. The trees bear continuously, two or three crops being collected yearly. The fleshy pericarp is first removed, then the arillode, which when dried constitutes mace; the seeds are dried, which requires from three to six weeks, after which the brittle testa is cracked off. With the exception of those from Penang, nutmegs are partially coated with lime to protect them from attacks by insects. Nutmegs were introduced into Europe by the Arabs about the middle of the twelfth century, but not until the sea routes

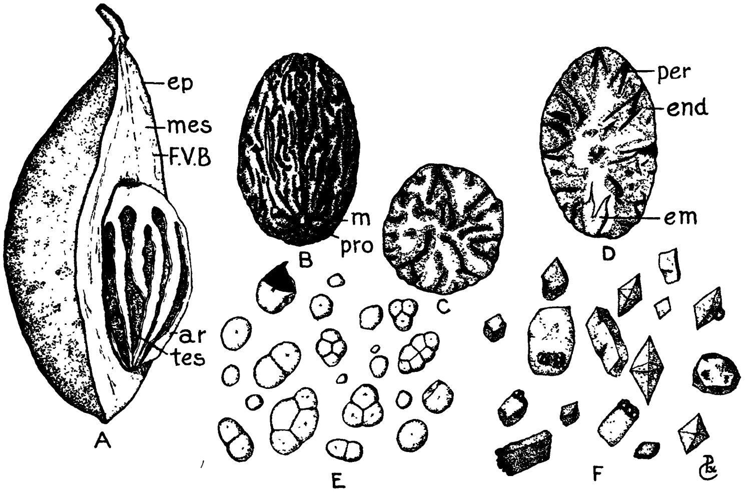


FIG. 138.—Myristica. *A*, fruit with half of the pericarp removed: *ep*, epicarp; *mes*, mesocarp with fibrovascular bundles (*FVB*); *ar*, the fleshy, branched, brilliantly red arillode which when separated and dried constitutes mace; *tes*, testa of seed. *B*, the kernel of the seed or whole nutmeg (the testa having been removed after the seed was dried); ovoid or ellipsoidal, 20 to 30 mm. in length, 15 to 20 mm. in diameter; externally light brown, or whitish from a dressing of lime, and reticulately furrowed; at one end a white, smooth projection (*pro*) 3 to 5 mm. in diameter, in the center of which is the micropyle (*m*), the chalaza being indicated near the other end by a slight, dark depression from which there extends a more or less distinct furrow, indicating the position of the raphé; easily cut, the surface having a waxy luster, and mottled by reason of the dark brown perisperm (*per* in *C* and *D*, views of the transverse and longitudinal median sections) penetrating into the yellowish brown endosperm (*end*); the shrunken embryo (*em*) lying in an irregular cavity about 4 to 5 mm. in length, near the micropyle; odor and taste strongly aromatic and pleasant. *E*, starch, the individual grains 3 to 22 microns in diameter; and *F*, aleurone from nutmeg showing large rhombohedral protein prisms; both *E* and *F* shows about 250 magnification. (Drawing by P. D. Carpenter.)

to the Indies were opened in the sixteenth century did they become a prevailing article of commerce. They played an important part in the Dutch spice monopoly until the tree began to be cultivated in other parts of the world (1800 A.D.)

DESCRIPTION, STRUCTURE AND POWDER.—See Figure 138 and the U. S. Pharmacopœia.

CONSTITUENTS.—Fixed oil, 25 to 40 per cent, solid at ordinary temperatures, sometimes occurring in prismatic crystals, and known as "Nutmeg Butter;" volatile oil, 8 to 15 per cent; proteins in considerable amounts; and starch.

STANDARDS.—Nutmeg contains not less than 25 per cent of non-volatile ether extract, not more than 10 per cent of crude fiber, not more than 5 per cent of total ash, and not more than 0.5 per cent of acid-insoluble ash.

USES AND DOSE.—Myristica is a condiment, an aromatic and a carminative. Average dose, 0.5 gm.

ADULTERANTS.—Kernels that are wormy or more or less broken should be rejected. Imitation nutmegs have been made by molding the exhausted powder or other substances into forms resembling nutmeg. These can be distinguished on cutting into the kernel; or, if it is made from a powder, on placing it in water it will immediately disintegrate. During Colonial times, when spices were expensive luxuries, imitation nutmegs were made in Connecticut, being carved out of basswood and colored like nutmegs.

ALLIED PRODUCTS.—**Macassar Nutmeg or Papua Nutmeg** is the dried seed of *Myristica argentea,* deprived of its testa. Other species of *Myristica* yield nutmegs which are used by the natives, as *M. succedanea* of Timor, *M. fatua* of the Indian Archipelago, and *M. kombo* of Guinea. The kernels of the seeds of *M. fatua* constitute the **long, wild, or male nutmeg.** They are narrow-ellipsoidal, feebly aromatic and have a more or less disagreeable taste. The seeds of *M. officinalis* and *M. bicuhyba* of Brazil have medicinal properties, a balsam being obtained from the latter and used as a substitute for copaiba. The so-called African nutmegs derived from *M. surinamensis* of the West Indies soon lose their odorous properties. *M. sebifera* of Guiana yields a fixed oil which has but little odor of nutmeg. Fatty and ethereal oils resembling those of nutmeg are found in the "American nutmegs" obtained from *Cryptocarya moschata* (Fam. *Lauraceæ*) of Brazil.

Myristica Oil, or Oil of Nutmeg (U. S. P. 1820 to date) is the volatile oil distilled from Myristica.

DESCRIPTION AND TESTS.—Oil of nutmeg is a colorless or pale yellow liquid having the characteristic odor and taste of nutmeg. It is soluble in an equal volume of alcohol and in three volumes of 90 per cent alcohol; specific gravity, 0.880 to 0.910 at 25° C.; optical rotation, +10° to +30° in a 100-mm. tube at 25° C.; refractive index, 1.474 to 1.488 at 20° C. Upon evaporation on a water-bath the oil should yield a residue not greater than 2 per cent.

USES AND DOSE.—A carminative and flavoring agent; externally a parasiticide. Average dose, 0.03 cc.

Mace (U. S. P. 1851 to 1905; N. F. 1916 to 1926) is the arillode of the seed of *Myristica fragrans* Houttuyn. According to Warburg, the arillode arises in the region of the hilum before the flower opens and fertilization is effected. The mace, as it occurs on the seeds (see Nutmeg) recently collected is of a brilliant red color. It is removed by hand, dried in the sun and acquires a yellowish or orange-brown color. It is usually shipped to Java or Singapore for exportation. The genuine article is usually referred to as Banda Mace.

Mace occurs in coarsely reticulate bands about 1 mm. in thickness, the whole having the outline of the nutmeg, the basal portion united, but with a small, irregular opening; usually in compressed nearly entire pieces, reddish or orange-brown, somewhat translucent, brittle when dry; and with an aromatic odor and taste.

For the structure see Figure 139.

The powder is yellowish- or orange-brown; very oily and with an aroma resembling nutmeg, but more delicate. Potassium hydroxide in solution added to the sections liberates the oil, producing a yellow color. The use of concentrated sulfuric acid in a similar manner, dissolves the oil, imparting to the globules a light orange-red color, which is more or less permanent and does not become reddish brown.

Mace contains an aromatic balsam 24.5 per cent; volatile oil 4 to 7 per cent, containing a larger percentage of terpenes than nutmeg oil; fixed oil; starch; and from 2 to 4 per cent of dextrogyrate sugar.

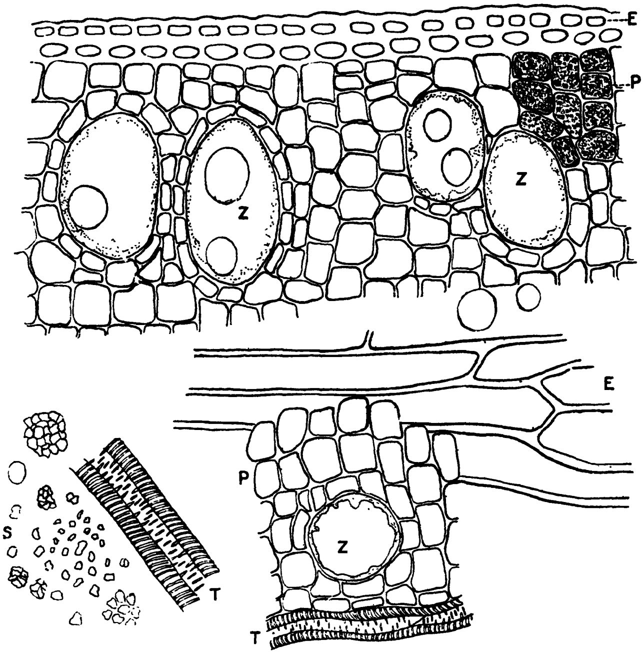


FIG. 139.—Mace: *E*, epidermal cells, which in transverse section are nearly isodiametric, but in longitudinal section are elongated, sometimes being 1 mm. in length; *P*, parenchyma cells with small starch grains which are colored reddish with iodine (amylodextrin); *Z*, large oil cells up to 65 microns in diameter, and showing oil globules and protoplasmic contents lining the walls; *T*, tracheæ; *S*, small, irregular starch grains up to 10 microns in length.

Mace contains not less than 20 per cent and not more than 30 per cent of non-volatile ether extract, not more than 10 per cent of crude fiber, not more than 3 per cent of total ash and not more than 0.5 per cent of acid-insoluble ash.

Mace is a condiment, an aromatic and a carminative. Average dose 0.5 gm.

ALLIED PRODUCTS.—**Macassar or Papua Mace,** derived from *Myristica argentea*, is somewhat darker, with broader segments than true mace, and possess an odor suggestive of methyl salicylate. It gives a cherry-red color with solutions of the alkalis or concentrated sulfuric acid, is very pungent and yields over 50 per cent of non-volatile ether extract and less than 10 per cent of starch.

Bombay Mace, or Wild Mace is the product of *Myristica malabarica;* it is distinguished from true mace in that the entire mace is narrow-ellipsoidal, the reticulations are not so coarse, the summit is divided into numerous narrow lobes and it is darker in color. With alkalis or sulfuric acid, wild mace assumes a darker red color than the true mace. It is slightly aromatic, but has little value as a spice and yields nearly 60 per cent of non-volatile ether extract.

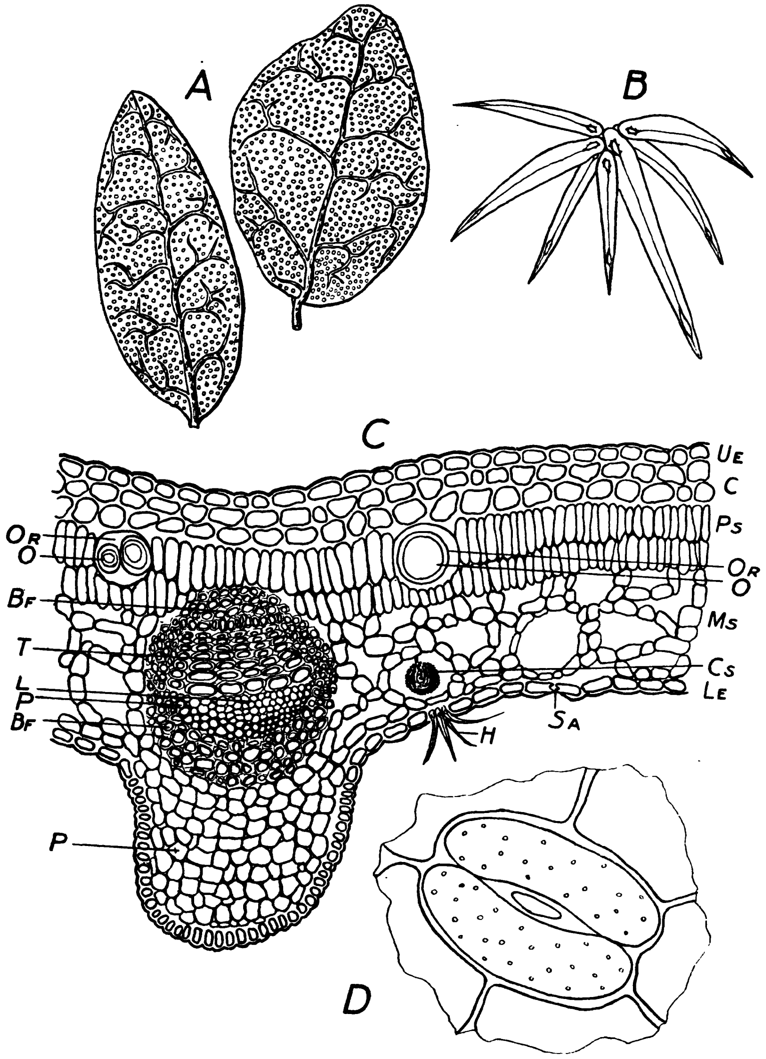


FIG. 140.—Boldo: *A*, leaves showing branching veins and small circular glandular punctations; *B*, a stellate hair with thick transparent walls; *C*, transverse section through the midrib showing upper epidermis (*Ue*); hypodermis (*C*); palisade layers (*Ps*); mesophyll (*Ms*); oil reservoirs (*Or*); containing oil globules (*O*); cystolith (*Cs*); a stellate hair (*H*); stoma (*Sa*); bast fibers (*Bf*); tracheæ (*T*); sieve (*L*); parenchyma (*P*); lower epidermis (*Le*); *D*, a stoma on the lower epidermis. (Drawing by Haase.)

Bombay mace is used to adulterate genuine mace and is usually suspected when a powdered article has a pronounced reddish color. It can readily be distinguished by its more numerous oil cells and the fragments being colored bright red upon mounting the powder in concentrated sulfuric acid or a solution of potassium hydroxide. When mounted in hydrochloric acid the fragments become greenish.

MONIMIACEÆ, OR MONIMIA FAMILY

The plants are mostly tropical trees or shrubs having opposite leaves and cymose flowers. They are especially distinguished by the presence of oil-secretion cells, which give an aromatic odor and a transparent dotting to the leaves (Fig. 140).

Boldo, or Boldus (N. F. 1916 to 1936) is the dried leaves of *Boldu boldus* (Molina) Lyons, an evergreen tree indigenous to Chili.

The leaves are broadly elliptical or ovate, 3 to 7 cm. in length, 1 to 5 cm. in breadth; with the apex acute, rounded, emarginate; the base acute or more or less rounded; the margin entire, distinctly revolute; the upper surface light green, with numerous small spherical projections and depressed veins; the under surface brownish green, the veins very prominent, pubescent, and the surface between the veins minutely and coarsely papillose; the petiole 1 to 5 mm. long; the texture coriaceous, brittle; the odor aromatic; and the taste aromatic and pungent.

For the structure see Figure 140.

The drug contains a volatile oil, 2 per cent; an alkaloid, boldine, which is bitter, very slightly soluble in water and soluble in alcohol, ether and chloroform, 0.1 per cent; a glucoside, boldoglucin; a resinous substance and tannic acid. Total ash about 9.45 per cent with about 5.95 per cent of acid-insoluble ash.

Boldo is an aromatic stimulant and mild diuretic. Average dose, 0.5 gm.

LAURACEÆ, OR LAUREL FAMILY

This is a family of aromatic shrubs and trees, comprising about 40 genera and 1000 species. They are mostly found in the tropics, although a few of the genera are rather common in the temperate regions. Oil-secretion cells are found in all parts of the plant, giving them a distinct fragrance. Many of the plants also contain mucilage cells. These may occur in the same parts of the plant as the secretion cells, and it has been suggested that there is a relationship between the two. It is well known that in those varieties of cinnamon which are deficient in oil there is an increase in the number of mucilage cells, and *vice versa*. The mucilage cells are usually somewhat elongated and are distributed in the palisade tissue of leaves and the cells of the inner bark and pith. The hairs are non-glandular, unicellular and occasionally sclerenchymatous. The stone cells of the inner bark are usually unequally thickened and frequently are U-shaped.

CINNAMON

Cinnamon was first recognized in the U. S. Pharmacopœia of 1820, using the plant name *Laurus cinnamomum*. Linné applied this name to the Ceylon cinnamon plant. In 1820 Cassia or Chinese cinnamon also was recognized under the name *Laurus Cassia*. The U. S. Dispensatory of 1833 states: "*Laurus cinnamomum* is a native of Ceylon where it

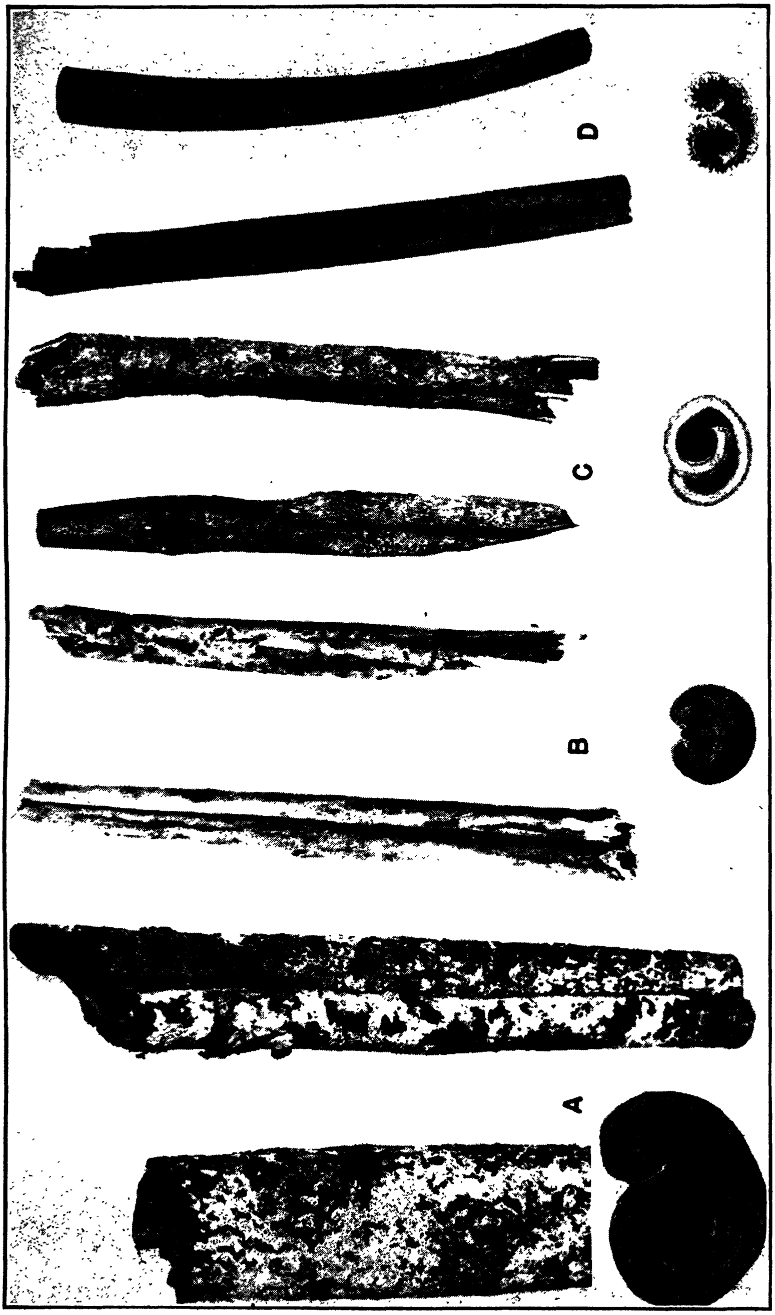


Fig. 141.—Cinnamon Bark Quills in longitudinal and transverse view. *A*, Saigon; *B*, Ceylon; *C*, Cassia and *D*, Batavia. (Photograph by Paul D. Carpenter.)

has long been cultivated for the sake of its bark. *Laurus cassia,* growing in China and Cochin China is considered by some authors as a distinct species. In odor and taste its bark resembles cinnamon bark, though less pleasant."

The Pharmacopœial recognition of cinnamon may be classified as follows:

Ceylon Cinnamon, U. S. P. 1820 to 1926; N. F. 1947 to date.
  Laurus cinnamomum Linné, U. S. P. 1820 to 1842.
  Cinnamomum zeylanicum Breyne, U. S. P. 1842 to 1926; *Cinnamomum zeylanicum* Nees, N. F. 1947 to date.
Cassia Cinnamon, U. S. P. 1820 to 1905.
  Laurus Cassia Aiton, U. S. P. 1820 to 1842.
  Cinnamomum aromaticum Nees, U. S. P. 1842 to 1882.
  Cinnamomum, undetermined species grown in China, U. S. P. 1882 to 1905.
Saigon Cinnamon, U. S. P. 1894 to date.
  Undetermined species of *Cinnamomum,* U. S. P. 1894 to 1926.
  Cinnamomum Loureirii Nees, U. S. P. 1926 to date.
Oil of Cinnamon or Oil of Cassia, U. S. P. 1820 to date.
  Laurus Cinnamomum Linné, U. S. P. 1820 to 1842.
  Cinnamomum zeylanicum Breyne, U. S. P. 1842 to 1894.
  Cinnamomum aromaticum Nees, U. S. P. 1842 to 1863.
  Cinnamomum Cassia Blume, U. S. P. 1882 to date.

The latest U. S. Pharmacopœial or National Formulary definitions of Cinnamon are as follows:

Cinnamon or Saigon Cinnamon is the dried bark of *Cinnamomum Loureirii* Nees.

Ceylon Cinnamon is the dried inner bark of cultivated trees of *Cinnamomum zeylanicum* Nees.

Cassia or Chinese Cinnamon is the bark of the shoots of one or more undetermined species of *Cinnamomum* grown in China.

Cinnamon Oil is the volatile oil distilled with steam from the leaves and twigs of *Cinnamomum Cassia* (Nees) Nees ex Blume, rectified by distillation.

An unofficial cinnamon found occasionally in U. S. commerce is **Batavia, Fagot or Java Cinnamon** obtained from *Cinnamomum Burmanni* Blume.

Cinnamon may be from the Arabic, *kinnamon;* or Malayese, *kaju manis* (sweet wood); or the Hebrew, *ginnamon. Loureirii* is in honor of the French botanist Loureiro; *zeylanicum* signifies Ceylon; *Cassia,* from the Greek *kassia* meaning "to strip off the bark." *Burmanni* refers to Johannes Burman, a Dutch botanist of note. *Saigon* is the capital of French Indochina; *Batavia* in Java is the capital of the Dutch East Indies.

Cinnamon as a spice is of great antiquity. It is named in the books of Moses, by the ancient Greek and Latin historians, and in Chinese herbals as early as 2700 B.C. Its cultivation in Ceylon probably dates from 1200 A.D.

The wild Cinnamon trees seldom exceed 30 feet (9 meters) in height. The leaves are coriaceous, green and glossy; the small flowers are in terminal panicles and the fruit is fleshy and ovoid.

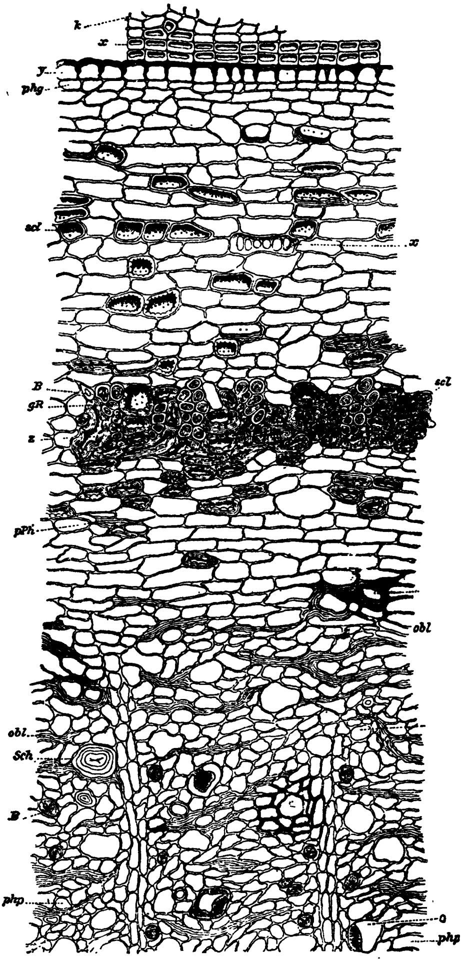


FIG. 142.—Transverse section of cassia cinnamon bark: *k*, cork; *x*, thick-walled lignified cork cells; *y*, cork cells, the outer walls of which are thickened; *phg*, phellogen; *scl*, stone cells; *x*, parenchyma cell with large pores; *B*, bast fibers; *gR*, short sclerenchyma; *z*, parenchyma separating the groups of sclerenchymatous tissue; *pPh*, protophloem; *obl*, collapsed sieve; *Sch*, mucilage canals; *php*, phloem parenchyma; *o*, oil cells. (After Tschirch and Oesterle.)

Practically all commercial cinnamon now is obtained from cultivated trees in Ceylon, southeastern China, French Indochina, Java and many other localities, including the West Indies. However, cinnamon from southeastern Asia and adjacent islands is superior in quality.

The bark is gathered from young trees usually under six years old and, in Ceylon, mostly from coppice shoots eighteen to thirty-six months old. The leaves, branches and stem tips are distilled with steam for the volatile oil. The bark is cut transversely and longitudinally and peeled. In Ceylon and Java it is scraped while fresh to remove epidermis and cork; in China it is planed to partially remove the cork. In Ceylon, after drying, many layers of the thin inner bark are rolled into one quill; in Java, several layers may be quilled together; and in China and Indochina each layer is quilled separately or but two or three layers together. Formerly, Chinese cassia from wild trees was in thicker, flat pieces known as **Cassia Lignea.**

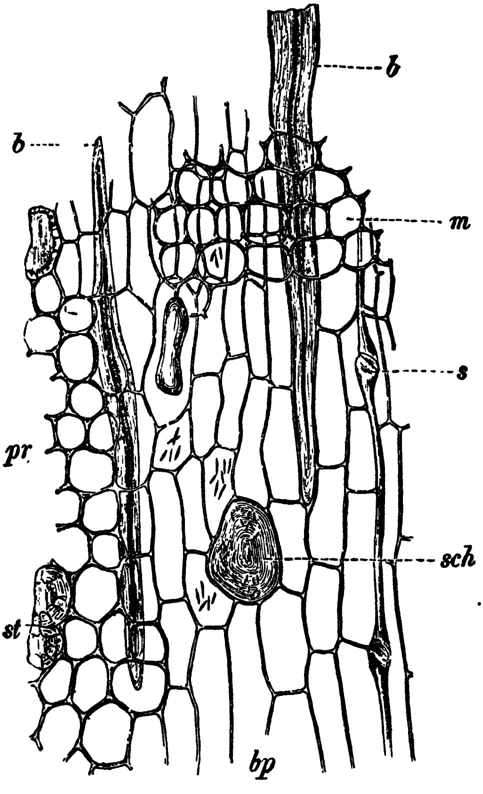


FIG. 143.—Radial-longitudinal section of cassia cinnamon bark: *pr*, parenchyma of outer bark; *bp*, parenchyma of the inner bark, some of the cells of which contain raphides; *b*, bast fibers; *st*, stone cells; *sch*, mucilage cells; *s*, sieve; *m*, medullary rays. (After Moeller.)

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 141, 142, 143, 144, the tabulation on page 274, the U. S. Pharmacopœia, and the National Formulary.

CONSTITUENTS.—Saigon cinnamon yields from 2 to 6 per cent of volatile oil, Cassia cinnamon 0.5 to 1.5 per cent, and Ceylon cinnamon 0.5 to 1 per cent of volatile oil. Other constituents are mannitol, to which the sweetness of the bark is due; mucilage, abundant in Batavia cinnamon; and tannin, more in Cassia cinnamon.

STANDARDS.—Saigon cinnamon yields not less than 2.5 per cent of volatile oil, and contains not more than 2 per cent of foreign organic matter. Total ash does not exceed 6 per cent.

USES.—Cinnamon is an aromatic, carminative and a mild astringent.

Important differences between the four common cinnamons are given in the following table:

	Saigon	Ceylon	Cassia	Batavia
Form	Single quills	Compound quills	Single quills	Usually double quills
External surface	Unscraped	Cork and cortex removed	Partially scraped	Scraped
Color of powder	Reddish brown	Light brown or yellowish brown	Reddish brown	Light reddish brown
Odor of powder	Aromatic, characteristic	Fragrant; delicately aromatic	Strongly aromatic	Weakly aromatic
Taste of powder	Aromatic and pungent	Warmly aromatic, delicate, and sweet	Aromatic, pungent and somewhat astringent	Aromatic and distinctly mucilaginous
Starch grains	Abundant, mostly over 0.010 mm.	Few, mostly under 0.010 mm.	Abundant, mostly over 0.010 mm.	Few, usually under 0.010 mm.
Cork cells	Present	Absent	Few	Absent
Fibers and stone cells	Fewer as compared with others	Abundant	More than Saigon, less than Ceylon	Abundant
Calcium oxalate	Raphides	Raphides	Raphides	Tabular and prismatic crystals

The powdered cinnamon found in the grocery trade is frequently a blend of several kinds of cinnamon. The blending is done either to improve the aromatic quality or to cheapen the product.

Aromatic Powder (U. S. P. 1820 to 1926; N. F. 1926 to date) is a mixture of cinnamon, 35 parts; ginger 35 parts; cardamom seed, 15 parts, and myristica 15 parts; reduced to fine powders and intimately mixed.

DESCRIPTION.—Moderate yellowish brown, with a strong, distinctive, aromatic odor; ginger starch grains numerous, ellipsoidal or ovoid, slightly beaked, and up to 60 microns in diameter; occasional stone cells; a few short calcium oxide raphides; a few fragments with sclerenchymatous fibers; numerous yellowish orange to reddish brown or darker fragments, with obscure cellular structure.

USES AND DOSE.—Aromatic stimulant and astringent internally; stimulant and anodyne externally as a fomentation. Dose, 1 gm.

Cinnamon Oil or Cassia Oil (U. S. P. 1820 to date) is the volatile oil distilled with steam from the leaves and twigs of *Cinnamomum Cassia* (Nees) Nees ex Blume, rectified by distillation.

Description.—Cinnamon Oil is a yellowish or brownish liquid becoming darker and thicker by age or by exposure to air, and possessing the characteristic odor and taste of cassia cinnamon; specific gravity, 1.045 to 1.063 at 25° C.; refractive index, 1.6020 to 1.6135 at 20° C.; optical rotation, +1° to −1° in a 100 mm. tube at 25°.

Constituents.—The principal constituent of the oil is cinnamic aldehyde, 75 to 85 per cent, the balance of the oil consisting of terpenes and other compounds.

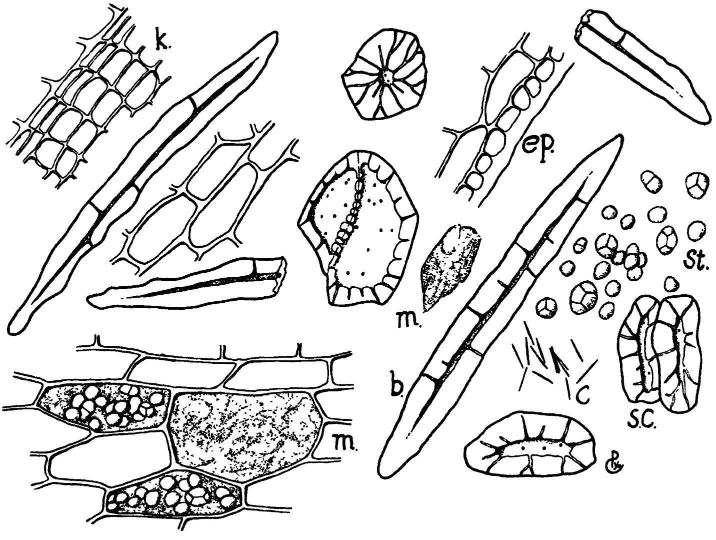


Fig. 144.—Powdered Cinnamon: *k*, fragment of cork, the cell walls somewhat lignified; *ep*, fragment of epidermis and parenchyma, the cuticle very thick and the parenchyma cell walls more or less brown, the cells containing an amorphous brown substance, starch, or calcium oxalate needles; *b*, fibers from 0.3 to 1.5 mm. in length with very thick, somewhat wavy lignified walls; *sc*, stone cells, irregular in shape and in wall thickness, with one wall often thinner than the other walls; *st*, starch grains, single and 2- to 4-compound and up to 25 microns in diameter; *c*, very small raphides of calcium oxalate. (Drawing by Paul D. Carpenter.)

To demonstrate cinnamic aldehyde in powdered cinnamon or in cinnamon oil, extract a few milligrams of the powder with about 1 cc. of chloroform, or dissolve a small drop of oil in 1 cc. of chloroform. Allow 2 drops of the chloroformic solution to evaporate on a slide. Add 2 drops of a 10 per cent aqueous solution of phenylhydrazine hydrochloride and cover with a cover-glass. Small rod-shaped crystals of the phenylhydrazone of cinnamic aldehyde soon appear.

Standards.—Oil of cinnamon contains not less than 80 per cent by volume of the total aldehydes of cinnamon. Oil of cinnamon should contain no *rosin, rosin oil, heavy metals* or *chlorinated products*, the detection of all of which are described in the Pharmacopœia.

Uses and Dose.—Oil of cinnamon is used as a flavoring agent, a carminative and pungent aromatic. It also has antiseptic properties. Average dose, 0.1 cc.

Cinnamaldehyde, Cinnamic Aldehyde or Cinnamyl Aldehyde (U. S. P. 1905 to 1916; N. F. 1947 to date) contains not less than 98 per cent of C_8H_7CHO.

Cinnamaldehyde is obtained from Cassia Oil or synthetically from a mixture of benzaldehyde and acetaldehyde by the action of sodium hydroxide.

Description.—It is a yellow, strongly refractive liquid with a cinnamon-like odor and an aromatic, burning taste. It forms a clear solution in 7 volumes of 60 per cent alcohol and is miscible with alcohol, chloroform, ether and fixed or volatile oils. Specific gravity at 25° C. is 1.048 to 1.052. Refractive index at 20° C. is 1.618 to 1.623.

It should be stored in well-filled, tight, light-resistant containers protected from excessive heat.

Cassia Buds are the immature fruits of *C. Loureirii*, and *C. Cassia*. The latter are club-shaped, 5 to 10 mm. in length, with a short stem or pedicel, externally dark brown, the 6-lobed perianth folded over the depressed and smooth ovary. The powder is characterized by numerous thick-walled, irregularly curved simple hairs; fragments of reticulate and scalariform tracheæ; and broad, blunt bast fibers. The odor is aromatic; taste pungent, aromatic and astringent. Cassia buds yield a volatile oil containing cinnamic aldehyde, which resembles that of cassia cinnamon.

Cayenne Cinnamon is the bark of cultivated plants of *Cinnamomum zeylanicum* grown in Guiana, Brazil and some of the islands of the West Indies. It is obtained from larger branches than that produced in Ceylon, and is said to be inferior to it in quality. It is a rare article.

Oliver Bark or Black Sassafras, the bark of *C. oliveri*, a native of Queensland, yields a volatile oil containing safrol. It is used locally as a cinnamon substitute.

Wild Cinnamon, the bark of *Cinnamomum pedatinervum*, a tree indigenous to the Fiji Islands, yields a volatile oil containing from 40 to 50 per cent of linalool and safrol, 15 to 20 per cent of a terpene, 1 per cent of eugenol and about 3 per cent of eugenol-methyl-ether.

Clove Bark, or Cassia Caryophyllata, is obtained from *Dicypellium caryophyllatum*, a tree indigenous to Brazil. The bark comes in long quills, consisting of 6 to 10 pieces of the scraped bark. Externally dark brown or purplish brown; fracture short, with a circle of whitish stone cells near the periderm; odor clove-like; taste mucilaginous and aromatic, resembling that of cinnamon.

CAMPHOR

Camphor (U. S. P. 1820 to date) is a ketone obtained from *Cinnamomum Camphora* (Linné) Nees et Ebermaier (Natural Camphor); or produced synthetically (Synthetic Camphor). *Camphora* is from the Arabic *kafur*, meaning chalk. The plant is a large evergreen tree (see Fig. 145) indigenous to eastern Asia but naturalized in the Mediterranean region, Ceylon, Egypt, South Africa, Brazil, Jamaica, Florida and California. Before World War II, about 80 per cent of the world's supply of natural camphor (about 4,000,000 kg. per year) was produced in Formosa, where the tree occurs naturally in abundance and is also extensively cultivated, the remaining 20 per cent being produced largely in Japan proper and southern China. Early references to camphor do not refer to the laurel camphor but rather to the Borneo camphor (see page 279) which reached Arabia in the sixth century and Europe in the twelfth. Laurel camphor appeared in Europe about the seventeenth century. On the Japanese annexation of Formosa, a government monopoly was created (1900). Since that time, however, the production of synthetic camphor has gradually lessened the demand for the Japanese product.

Natural camphor occurs as a crystalline product in clefts in the wood of the stems and roots, and to a greater extent dissolved in the volatile oil. The wood is chipped and distilled with steam, usually in a rather crude way in a wooden tub with a perforated bottom over an iron kettle containing water and set in a masonry furnace. The steam passes through the tub filled with chips, conveys the camphor and volatile oil into the condensing tubs. About twelve hours are required to distil a charge, and 1 pound of crude camphor is obtained from 20 to 40 pounds of chips. The crude camphor is then freed of oil by centrifugation and pressing, and finally resublimed in chambers where it condenses in small crystals which are pressed into the familiar cakes. The crude camphor was formerly sent to Europe or America for refining, but since 1900 a considerable amount of the refining has been done in Japan.

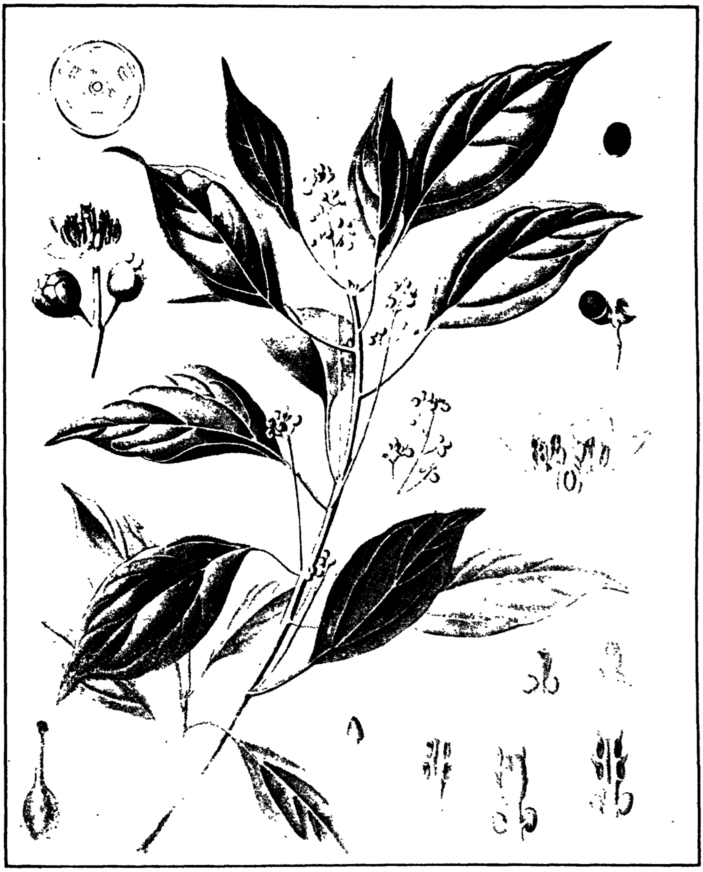


FIG. 145.—*Cinnamomum camphora.* (After Köhler.)

Before World War II, about 6,500,000 kg. of synthetic camphor were produced annually in Europe and United States. During this war the production of synthetic camphor has been so increased as practically to replace natural camphor. With the conclusion of this war, and the restoration of Formosa to China, the production of natural camphor probably will be resumed, but whether it will largely replace the synthetic camphor remains a question.

Synthetic camphor is made from pinene, the principal constituent of turpentine oil. A number of methods have been used for producing synthetic camphor, rather highly complex chemically, but all based on: (1) converting pinene into bornyl esters, which are (2) hydrolyzed to isoborneol, and (3) this is oxidized to camphor.

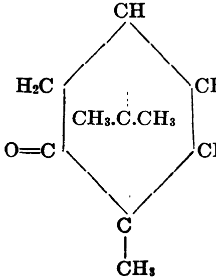
Description, Constants, and Tests of Identity and Purity.—See the U. S. Pharmacopœia. One gm. of camphor dissolves in about 800 cc. of water, in 1 cc. of alcohol, in 0.5 cc. of chloroform, in 1 cc. of ether, in 1.5 cc. of turpentine oil, in 4 cc. of olive oil; it forms a liquid when rubbed with equal parts of hydrated chloral, or phenol, or salicylic acid, or salol, or menthol, or naphthol, or pyrogallol, or resorincol, or thymol.

Camphor is readily pulverizable in the presence of a little alcohol, ether or chloroform. On heating some of the powder on a slide and covering with a watch crystal, a sublimate is obtained, composed of radiating aggregates of feather-shaped crystals, which are isotropic. A drop of a solution of vanillin (1 in 100) and a drop of sulfuric acid added to powdered natural camphor produces immediately a yellow color, changing to red, then violet and finally blue. Synthetic camphor gives no reaction.

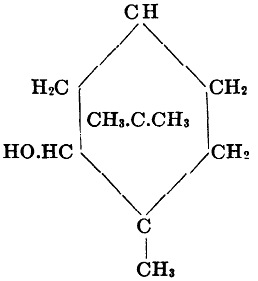
The specific rotation of natural camphor (see U. S. P.) is between +41° and +43°. The specific rotation of synthetic camphor is between +5° and −5°.

Constituents.—Camphor consists almost entirely of a dextrogyrate modification of the saturated ketone, $C_9H_{16}CO$.

The structural formulas of both camphor and borneol are given to illustrate their relationship.



Camphor



Borneol

Standards.—Camphor should be free from water (determined by the clarity of its solution in petroleum benzin) and from halogens and should sublime without carbonization, leaving no more than 0.05 per cent of non-volatile matter. Stearic acid has been found as an adulterant of camphor. It can be detected by preparing a solution of 1 gm. of the camphor mixture in 1 cc. of alcohol. The stearic acid remains mostly undissolved.

Uses and Dose.—Camphor is a stimulant and antispasmodic. Externally it is antiseptic and rubefacient. A great deal of camphor is used in the manufacture of celluloid. Average dose, 0.2 gm. (by mouth or hypodermically).

Monobromated Camphor (U. S. P. 1882 to 1926; N. F. 1936 to date) is made by the action of bromine on camphor; it is composed of camphor about 65 per cent and bromine 35 per cent.

Description.—Colorless or prismatic needles or scales, with a mild, camphoraceous odor and taste; readily soluble in alcohol, chloroform or ether; nearly insoluble in water; melting point 74° to 76° C.

Uses and Dose.—It is a nerve sedative and an anaphrodisiac. Dose, 0.125 gm.

Camphor Oil, Formosa, Japanese, White or Light Oil of Camphor (U. S. P. 1863 to 1882) is the volatile oil from *Cinnamomum Camphora.*

Camphor Oil is a colorless or yellowish liquid, with an odor of camphor; it is insoluble in water, but readily soluble in 3 volumes of alcohol and in ether, chloroform and oils.

Camphor Oil consists largely of safrol; that portion of the oil boiling near 230° C. is separated as **Artificial Oil of Sassafras.**

Camphor Oil is a stimulant, rubefacient, antiseptic and parasiticide.

Borneo Camphor or Borneol (see formula above) is a product found in clefts of the wood of *Dryobalanops camphora* (Fam. *Dipterocarpaceæ*), a large tree indigenous to Borneo and Sumatra. The camphor is obtained by scraping the wood and not by distillation. It somewhat resembles true camphor, but is distinguished by being heavier than water, not volatilizing at ordinary temperatures, and having a somewhat pungent taste. It is a secondary alcohol and is converted by nitric acid into true camphor. It should also be stated that true camphor when treated with reducing agents is converted into Borneo camphor. The latter is seldom seen in commerce on account of its high price.

Ngai Camphor is similar to true camphor and is obtained from *Blumea balsamifera* (Fam. *Compositæ*), a shrub growing in the Malay Peninsula. In California, camphor is produced from *Ramona stachyoides, Artemisia trifolium* and *Artemisia frigida,* all Composites.

SASSAFRAS

Sassafras or Sassafras Bark (U. S. P. 1820 to 1926; N. F. 1926 to date) is the dried bark of the root of *Sassafras albidum* (Nuttall) Nees (*S. variifolium* [Salisbury] O. Kuntze).

The plant is a tree indigenous to eastern North America. In the north it is commonly shrubby but farther south it attains a height of 20 to 30 meters. The leaves vary in form and size even on the same plant, some being ovate and entire, others 2- or 3-lobed; they contain a citral volatile oil, hence are pleasantly aromatic, resembling lemon. The stem bark contains a combination of the citral oil of the leaves and the safrol oil of the root bark. The root bark is gathered early in the spring or late in the fall, deprived of the outer corky layer and dried. Most of the commercial supplies come from Virginia, Tennessee and Kentucky. Sassafras was used medicinally by the Seminole Indians in Florida long before Ponce de Leon set foot there in 1512. The records of De Soto's invasion of Florida in 1538 show no reference to the drug, the earliest detailed description being that of the Spanish physician Monardes (1574).

Description, Structure and Powder.—See Figure 146 and the National Formulary.

Constituents.—Volatile oil 5 to 9 per cent, and containing about 80 per cent of safrol; tannin about 6 per cent; a reddish brown altered tannin compound (sassafrid), about 9 per cent; resin and starch.

Standards.—Sassafras yields not less than 4 cc. of sassafras oil from each 100 gm. of drug; it contains not more than 4 per cent of adhering wood or other foreign matter; and yields not more than 5 per cent of acid-insoluble ash.

Uses and Dose.—Sassafras is an aromatic, an alterative and a carminative. Average dose, 10 gm.

Sassafras Pith (U. S. P. 1831 to 1916; N. F. 1916 to 1936) is the dried pith of *Sassafras varifolium* (Salisbury) O. Kuntze. It is gathered late in autumn and contains a mucilage which is not precipitated by alcohol. A decoction of the drug is used as a demulcent in eye lotions and in gastro-intestinal irritations.

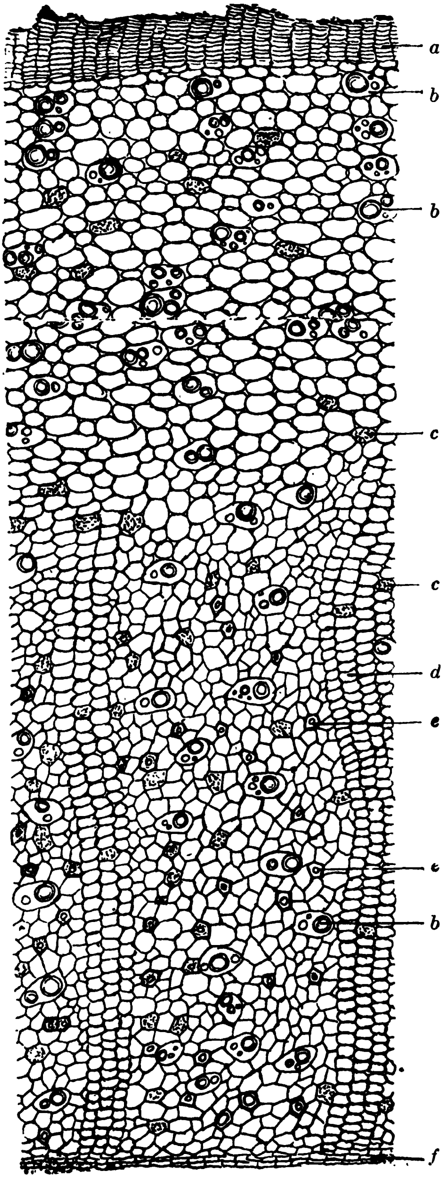


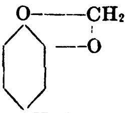
FIG. 146.—Transverse section of root bark of Sassafras: *a*, cork; *b*, oil cells; *c*, tannin cells; *d*, medullary rays; *e*, bast fibers; *f*, cambium. (After Bastin.)

Sassafras Oil (U. S. P. 1820 to date) is the volatile oil distilled with steam from the root of *Sassafras albidum* (Nuttall) Nees. The oil is distilled from the entire root rather than the root bark. Being heavier than water, it sinks to the bottom of the receiving vessel.

Description.—A yellow or reddish yellow liquid having the characteristic odor and taste of sassafras; specific gravity, 1.065 to 1.077 at 25° C.; optical rotation +2° to +4° in a 100 mm. tube at 25° C.; refractive index 1.525 to 1.535 at 20° C. Oil of sassafras should be free from heavy metals.

Sassafras Oil tends to congeal at low room temperatures; if this occurs, carefully warm it at a low temperature until it is liquified, then thoroughly mix it before dispensing.

Safrol (U. S. P. 1905 to 1916) is the phenolic ether,



It is abundant in camphor oil, from which it was first isolated in 1885, and in sassafras oil; it is also found in the volatile oil from the fruits of *Illicium religiosum* (see page 263).

Safrol is a colorless or yellow liquid with the sassafras odor, boiling at 232° to 234° F. and solidifies at about 11° C. It is insoluble in water, but readily soluble in alcohol, chloroform, ether, etc.

Uses and Dose.—Sassafras Oil and Safrol are carminative and stimulant. Both are used as a flavoring in confections and pharmaceutical preparations. also in perfumery, especially for soaps. Average dose 0.1 cc.

Safrol may be readily converted into isosafrol, which upon oxidation, yields the aldehyde **piperonal (heliotropin)** used in perfumery (see page 188).

True Coto Bark is the bark of *Nectandra coto*, a tree growing in Bolivia. The bark occurs in flattened or curved pieces, from 7 to 20 mm. in thickness; the outer surface is reddish brown, nearly smooth or longitudinally fissured, occasionally with transverse clefts or grayish lichens, the smooth bark being marked with large lenticular lenticels; the inner surface is very coarsely longitudinally striate; the fracture is very tough; the fractured surface is light reddish brown, porous and shows numerous yellowish groups of sclerenchymatous cells and fibers; the odor is distinct, aromatic, somewhat camphoraceous, and the taste aromatic and pungent.

The bark contains a pale yellow volatile oil, having an aromatic odor and pungent taste; a light yellow crystalline glucoside, cotoin, 1.5 per cent, which is acrid and sternutatory, soluble in boiling water and alcohol, and which possesses the activity of the drug. Two new alkaloids have been isolated by Seil, a non-phenolic alkaloid, parostemine and a phenolic alkaloid, parosteminine, the two making up about 1.38 per cent of the bark.

Coto is used as a tonic and stomachic, particularly in atonic dysenteries. Average dose, 1 gm.

Paracoto, or Para-coto Bark (N. F. 1916 to 1926) is a bark of unknown origin, possibly derived from *Palicurea densiflora* (Fam. *Rubiaceæ*), a tree indigenous to Bolivia. It resembles coto bark and has a grayish or whitish periderm. The fracture is not so splintery, the odor is less aromatic, and the taste not so pungent. It contains paracotoin, which resembles cotoin in its physiological action; also hydrocotoin; protocotoin; methyl-hydrocotoin; methyl-protocotoin, diperonylic acid and tannic acid.

False Coto Bark is obtained from *Ocotea pseudo-coto* (Fam. *Lauraceæ*) and from *Cryptocarya pretiosa* (Fam. *Sapotaceæ*), a tree growing in the Amazon district. It occurs in pieces about 15 cm. in length, 5 cm. in width and 7 mm. in thickness; externally light brown and without cork; fracture short, fibrous; internally brown with yellowish groups of stone cells, which are arranged in radial rows, thus distinguishing this bark from true coto bark. The odor is slight, resembling that of cinnamon. It contains a brownish yellow volatile oil, with an odor suggestive of cinnamon, but it does not contain any cinnamic aldehyde. It also contains 0.145 per cent of an alkaloid.

Bay Laurel, the leaves and fruits of *Laurus nobilis,* are used as a spice.

PAPAVERACEÆ, OR POPPY FAMILY

This is a family of about 600 species, occurring most abundantly in north temperate regions. They are especially characterized by their milky and frequently yellowish latex, which arises either in laticiferous vessels or in special laticiferous sacs. The former are found in *Papaver,* and consist of tubes formed as a result of the fusion of cells in close proximity to each other, the dividing walls having become absorbed. The laticiferous sacs, which are present in *Chelidonium,* are either spheroidal or more or less cylindrical, elongated cells having very thin walls, and occur either isolated or arranged in longitudinal chains. The tracheæ in this family are marked by simple pores. Calcium oxalate does not occur, except in *Bocconia.* Non-glandular hairs, when present, consist of a chain of cells. Glandular hairs have not been observed in this family.

OPIUM

Opium or Gum Opium (U. S. P. 1820 to date) is the air-dried, milky exudation obtained by incising the unripe capsules of *Papaver somniferum* Linné or its variety *album* DeCandolle. The term *opium* is from the Greek *opion,* meaning poppy juice; *papaver* is the Latin name for the poppy and *somniferum* is Latin meaning to produce sleep.

The opium poppy is an annual herb with large, showy, solitary flowers varying in color from white (var. *album*) to pink or purple. It is native to Asia Minor, was introduced into India by the Mohammedans in the fifteenth century and cultivation was begun in Macedonia and Persia about the middle of the nineteenth century. Opium is commercially produced now in Turkey, the Balkan States, Persia, India and China. The discovery of the medicinal qualities of opium is lost in antiquity. Theophastus (third century B.C.) mentions it, and Dioscorides (A.D. 77) distinguishes between the juice of the poppy and an extract of the entire plant. In 1806 Sertüner first isolated the alkaloid morphine from opium.

CULTIVATION, COLLECTION AND COMMERCE.—The seeds of the opium poppy are sown in October in well-cultivated soil. The seeds germinate in the fall and the seedlings may be an inch high when snow falls; this protects them from freezing. In the spring when the plants have attained the height of 6 inches, the fields are cultivated and the plants thinned to stand about 2 feet apart. The poppy blossoms in April or May and the capsules mature in June or July. Each plant bears from 5 to 8 capsules.

The ripening capsules, about 4 cm. in diameter, change from bluish green to yellowish in color. This is a critical time for collecting the latex. The capsules are incised with a knife, usually three-bladed, the incision being made around the circumference of the capsule. The latex tubes open into one another so that it is not necessary to incise them all. Great skill, however, is required so as not to cut through the endocarp, in which case the latex would flow into the interior of the capsule and be lost. The latex, which is at first white, rapidly coagulates and turns brown. This is removed early the following morning, being scraped off with a knife and transferred to a poppy leaf. When sufficient latex is collected it is kneaded into balls which are wrapped in poppy leaves and shade dried. The opium is then inspected and usually packed with the brown winged fruits of a *Rumex* which prevents cohering. In some districts the latex is molded or pressed into cakes or other forms which are then wrapped in paper.

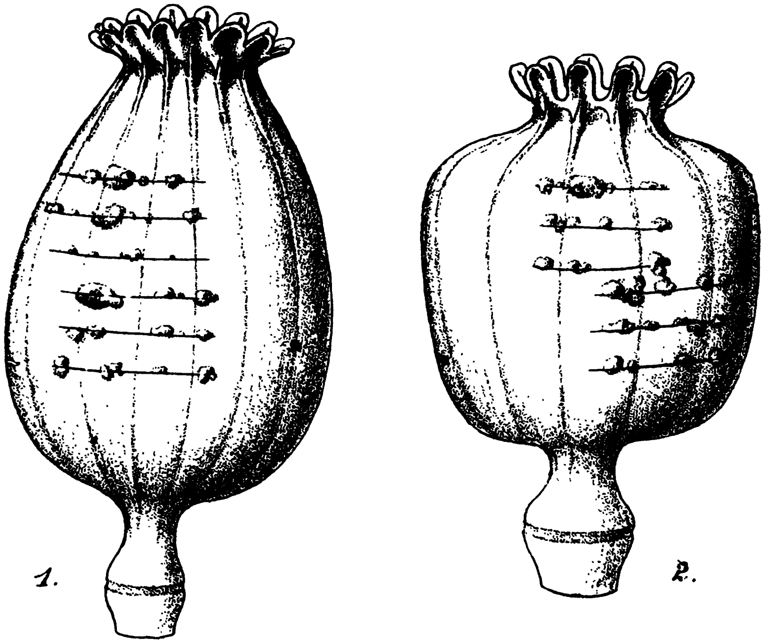


FIG. 147.—Poppy capsules grown in the gardens of the Pharmaceutical Institute of the University of Berlin in Dahlem, Germany. Two of the capsules grown from white seeds showing the transverse incisions from which the milk juice exudes, forming irregular globular masses on the surface of the capsules. (After Thoms.)

DESCRIPTION.—In more or less rounded, somewhat flattened masses, usually about 8 to 15 cm. in diameter; externally dark brown, covered with fragments of poppy leaves and at times with fruits of a species of *Rumex* adhering from the packing; more or less plastic when fresh, becoming hard and brittle or tough on keeping; internally, coarsely granular or nearly smooth, dark brown, frequently interspersed with lighter areas, somewhat lustrous; odor characteristic, narcotic; taste very bitter, characteristic.

The principal commercial varieties are as follows:

1. **Turkey Opium** most closely conforms to the description in the U. S. Pharmacopœia and is the one generally used for pharmaceutical purposes. It is produced in Turkey, Asia Minor, Bulgaria and Macedonia, the principal ports of export being Constantinople and Smyrna. The term "Druggists' Opium" is often applied to Turkey opium containing from 10 to 20 per cent of moisture. "Soft" or "Shipping" opium are names applied to Turkish or Balkan opium having a pasty consistency and containing about 30 per cent of moisture. This grade has a high morphine content (10 to 21 per cent) and is imported for alkaloid manufacture. It never appears on the market for pharmaceutical purposes.
2. **Persian Opium** is rarely seen in the American market. It occurs in brick-shaped cakes having a more homogeneous texture than Turkey opium. When

dry it is extremely hard, due possibly to the addition of gum during its manufacture. It contains from 4 to 12 per cent of morphine. The cakes weigh about 500 gm. and are usually wrapped in red paper.

3. **Indian Opium** is produced at Ghazipur and is consumed in India or exported for British trade. It occurs in cubes wrapped in oiled paper and weighing about a kilo, or in balls weighing about 1.5 kg. It yields up to 13 per cent of morphine.

4. **Chinese Opium** is produced on a large scale in China but is not exported. It occurs in flat globular cakes usually wrapped in paper and contains from 4 to 11 per cent of morphine.

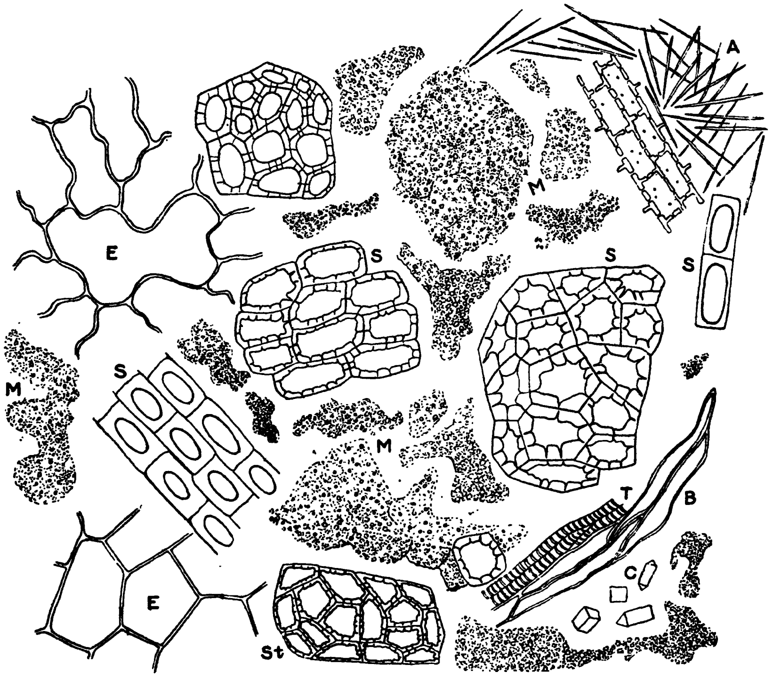


FIG. 148.—Powdered Opium: light brown; grayish brown, irregular, granular fragments (*M*), 15 to 170 microns in diameter, of protoplasm-like latex constitute the greater portion of the powder as mounted in glycerin; *S*, *St*, thick-walled, polygonal cells of the capsule epidermis; *E*, epidermal cells of rumex leaves, somewhat polygonal in surface view with occasional elliptical stomata about 70 microns in length; brown fibrovascular tissue composed of spiral tracheæ (*T*) and narrow sclerenchymatous fibers (*B*) from the wings of rumex fruits; *A*, needle-shaped crystals which sometimes separate in chloral-iodine mounts; *C*, crystals (probably of calcium oxalate). Turkey opium has the largest number of epidermal cells of the capsule, Indian opium few or none, and Persian opium very few. Starch is usually absent except in Persian opium, where an appreciable amount is present, or when starchy material has been used as a diluent of the powdered opium. Other microscopic characteristics of diluents may also appear.

5. **Egyptian Opium** was formerly an article of commerce. Egypt has however discontinued the production of opium.

CONSTITUENTS.—A large number of alkaloids have been obtained from opium and its extracts, some of which are, no doubt, alteration products of the alkaloids naturally occurring in the drug; the most important of these is morphine, which exists to the extent of 4 to 21 per cent.

Opium also contains from 3 to 5 per cent of **meconic acid**, which exists free or in combination with morphine, codeine and other alkaloids. It forms rhombic prisms, which are soluble in water and alcohol and give a deep red color in solutions of ferric chloride, which is not altered on the addition of diluted hydrochloric acid. Since meconic acid is found only in opium, this test may be used for the detection of opium. The total ash yield of opium is from 4 to 8 per cent, with about 0.65 per cent of acid-insoluble ash.

STANDARDS.—Opium in its normal, air-dried condition yields not less than 9.5 per cent of anhydrous morphine.

USES AND DOSE.—Opium acts chiefly upon the central nervous system, its action first stimulating then depressing nerve response. It is an analgesic, a hypnotic, and a narcotic; it checks excessive peristalsis and contracts the pupil of the eye. Average dose, 60 mg.

ADULTERANTS.—Fragments of the capsules, the pulp of figs and other fruits, tragacanth, beeswax, powdered cumin seed, starch and various inorganic substances, as clay, sand, stone, lead piping, lead bullets, etc., have been found in opium. While starch is not usually admixed with Turkish opium, it is nearly always present in the Persian variety.

Granulated Opium (U. S. P. 1905 to date) and **Powdered Opium** (U. S. P. 1882 to date) yield not less than 10 per cent and not more than 10.5 per cent of anhydrous morphine. Granulated opium or powdered opium of a higher morphine percentage may be reduced to the official standard by admixture with granulated or powdered opium of a lower percentage, or with any of the diluents permitted for powdered extracts. The diluents may be colored with caramel to simulate the color of the drug.

Granulated opium is used in making Tincture of Opium, and powdered opium in Dover's Powder.

Deodorized Opium, or Denarcotized Opium (U. S. P. 1882 to 1926) is powdered or granulated opium macerated and percolated with purified petroleum benzin, until the latter passes through without color. Strong ethyl ether was used originally instead of the benzin. This process removes the narcotine, at one time considered as a highly narcotic alkaloid of opium but now considered non-narcotic. The drug meets the standards of powdered opium.

Ipecac and Opium Powder or Dover's Powder (U. S. P. 1820 to 1942; N. F. 1942 to date) consists of finely powdered ipecac, 10 parts, powdered opium 10 parts, and coarsely powdered lactose 80 parts. These are triturated together until the mixture is reduced to a very fine powder.

DESCRIPTION.—The powder is very pale brown and consists mostly of coarse, angular, sometimes cone-shaped, colorless fragments, up to 400 microns in length, soluble in water and solutions of hydrated chloral, and very strongly polarizing with a rich display of colors (*fragments of lactose*); numerous starch grains and occasional tracheid fragments of ipecac (see page 606), and occasional fragments with the tabular characteristic stone cells of the opium poppy capsules, with their light brown, porous and strongly lignified walls, and other elements found in powdered opium, including tissues of the permissible diluents. Lactose may further be identified by its phenylosazone (see page 131), and opium by the ferric chloride test for meconic acid.

USES AND DOSE.—Ipecac and opium powder is a diaphoretic. Opium augments the effect of ipecac by dilating the vessels of the skin. Average dose, 0.3 gm.

Papaver, or Poppy Capsules (U. S. P. 1842 to 1882; N. F. 1916 to 1926) are the dried, full-grown, unripe fruits of *Papaver somniferum* or its variety *album.* The capsules are gathered in July, when they are full grown but still green and contain their milky juice. They are carefully and rapidly dried over a low-burning fire. The capsules are ellipsoidal, ovoid or depressed globular (see Fig. 147), from 6 to 7 cm. in length and from 4 to 7 cm. in diameter; very light, each weighing from 3 to 4 gm.; summit crowned by the 12- to 18-rayed stigma; base usually tapering into the stalk; externally yellowish brown or light brown, often marked with bluish black patches and slight ridges, indicating the dissepiments; unilocular, and containing numerous seeds; inner surface with numerous, thin, cartilaginous dissepiments, about 10 mm. in width, of a light yellowish brown color and marked by numerous small, circular, brownish spots, representing groups of stone cells; inodorous; taste bitter and slightly astringent. Poppy capsules contain from 0.13 to 0.36 per cent of a mixture consisting of morphine, codeine, narcotine and other opium alkaloids. During ripening the amount of morphine decreases while the percentage of codeine and narcotine increases. The drug possesses a sedative action in doses of 1 gm.

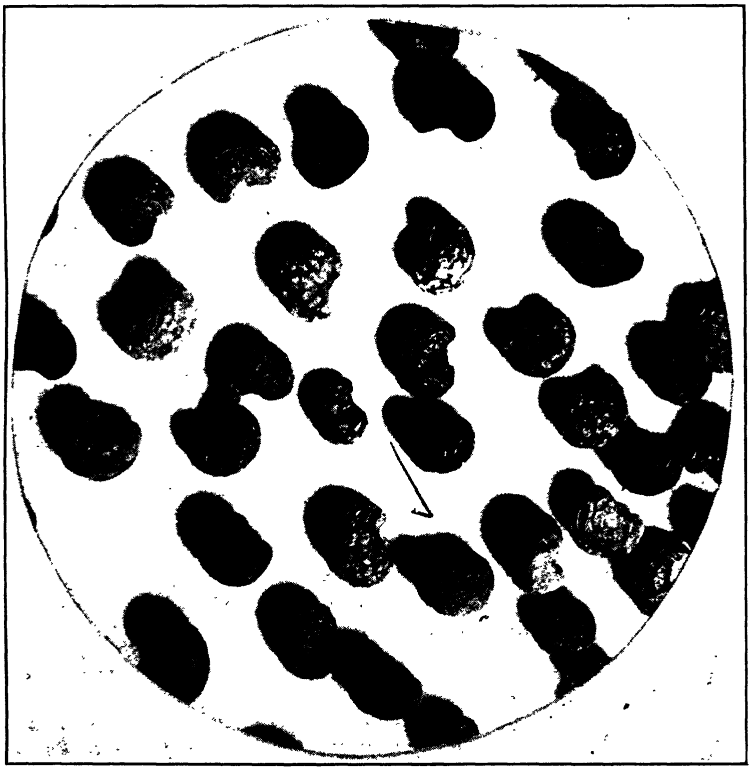


FIG. 149.—Black Poppy Seed in lens view. (Photo by Adamson.)

Poppy Seed or Maw Seed is the dried seed of *Papaver somniferum*. The seeds are bluish black or yellowish white, reniform (see Fig. 149), from 0.5 to 1 mm. in diameter, reticulate, with a yellowish hilum scar, white, oily endosperm and a curved embryo; taste slight and oily. Poppy seed are used in baking (poppy seed rolls). They contain about 50 per cent of a fixed oil (**Poppy Seed Oil**), which is used by artists as a drying oil, and also for food and salad dressings. **Poppy Seed Oil Cake** is used as a cattle food. Poppy seed contains no alkaloids.

Papaver Rhœas consists of the petals of the field poppy, *P. rhœas*. They are employed in Europe as a red coloring agent, the coloring material being an anthocyanin glucoside.

THE ALKALOIDS OF OPIUM

Morphine, U. S. P. 1831 to 1926
Morphine Acetate, U. S. P. 1831 to 1916.
Morphine Hydrochloride, U. S. P. 1842 to 1936; N. F. 1936 to date.
Morphine Sulfate, U. S. P. 1831 to date.
Codeine, U. S. P. 1882 to 1947; N. F. 1947 to date.
Codeine Phosphate, U. S. P. 1905 to date.
Codeine Sulfate, U. S. P. 1905 to date.
Ethylmorphine Hydrochloride, U. S. P. 1916 to date.
Diacetylmorphine (Heroin), U. S. P. 1916 to 1926.
Diacetylmorphine Hydrochloride, U. S. P. 1916 to 1926.
Apomorphine Hydrochloride, U. S. P. 1882 to date.
Papaverine Hydrochloride, N. F. 1936 to 1947; U. S. P. 1947 to date.
Cotarnine Chloride, U. S. P. 1916 to 1936; N. F. 1936 to date.
Dihydromorphinone Hydrochloride, U. S. P. 1942 to date.
Narcotine, Thebaine, Narceine, Protopine, Codamine, Cryptopine, Gnostopine, Lanthopine, Laudanine, Laudanosine, Meconine, Meconodine, and Xantholine have never been recognized in the U. S. Pharmacopœia or the National Formulary.

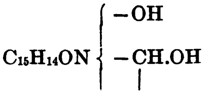
Morphine is the most important of the opium alkaloids. Morphine and the related alkaloids contain a phenanthrene nucleus and the various structural formulas which have been proposed are based on this fact. The molecule contains a phenolic and an alcoholic hydroxyl group.

Morphine and its salts occur as white, silky crystals, sometimes in cubical masses or as a fine crystalline powder, stable in air, odorless and with a bitter taste. The crystals of the sulfate formed on a slide from aqueous or alcoholic solutions are prismatic needles (see Fig. 150).

For the properties and tests of identity of morphine and its salts see the U. S. Pharmacopœia and the National Formulary. With Marme's reagent, morphine gives clusters of slender needles; with Wagner's reagent, large reddish brown plates; and with sodium carbonate, prisms of considerable size.

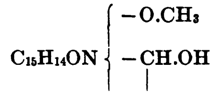
Morphine and its salts are strongly analgesic, hypnotic and narcotic, but very weakly stimulant. Their use tends to induce nausea, vomiting and constipation as well as habit-formation.

Codeine is obtained from opium (0.2 to 0.7 per cent) or prepared from morphine by methylation. Codeine is methyl morphine, in which the methyl group replaces the hydrogen of the phenolic hydroxyl group. The relation between morphine and codeine may be expressed as follows:



$$C_{15}H_{14}ON\left\{\begin{array}{l}-OH\\ -CH.OH\\ \quad\;\; |\\ -CH_2\end{array}\right.$$

Morphine



$$C_{15}H_{14}ON\left\{\begin{array}{l}-O.CH_3\\ -CH.OH\\ \quad\;\; |\\ -CH_2\end{array}\right.$$

Codeine (Methyl morphine)

Codeine and its salts occur in fine needles or in a white crystalline powder which effloresce in air. For other properties and tests of identity see the National Formulary and U. S. Pharmacopœia.

Among the microcrystalline reactions for codeine, Marme's reagent gives an amorphous precipitate which crystallizes rapidly into masses of small rods and these, upon standing, change to rosettes of rods and plates; potassium iodide gives long needles; chromic acid, dark spherical rosettes of plates; Wagner's reagent, rosettes of plates; and ammonium thiocyanate, large rosettes of rods with forked ends, which polarize brightly.

Codeine and its salts are used as sedatives especially in allaying coughs. While the action is similar to that of morphine, codeine is considerably less toxic and involves much less danger from habit formation. Average dose of codeine or its salts, 30 mg.

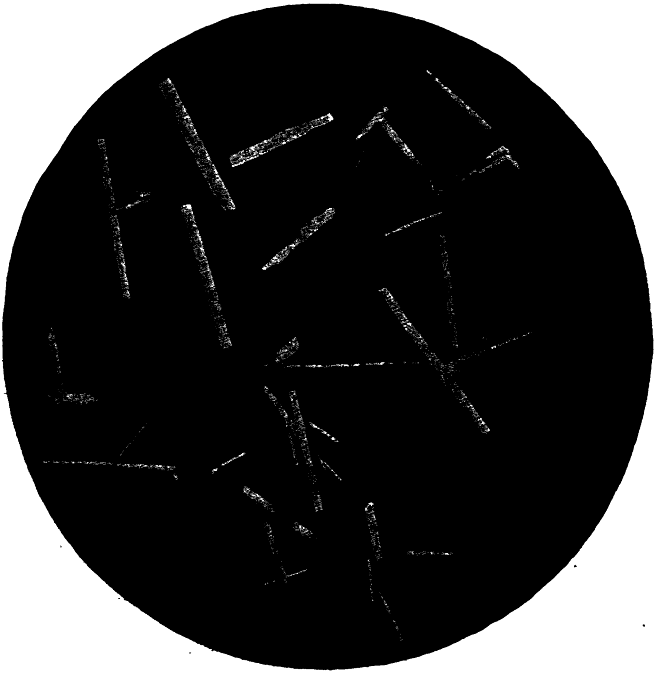


FIG. 150.—Morphine sulfate; orthorhombic crystals from aqueous solution.

Ethylmorphine Hydrochloride is the hydrochloride of a monoethyl ether of morphine It is prepared by treating morphine with ethyl iodide in alkaline solution. The compound is similar to codeine except that the hydrogen of the phenolic group of the morphine molecule is replaced by an ethyl group.

Ethylmorphine should be free from morphine, codeine and ammonium compounds (consult the U. S. Pharmacopœia for structure, tests, etc.).

The action of ethylmorphine is similar to that of morphine, except that it is less toxic and usually produces no constipation, nausea or lassitude. Average dose, 15 mg.

Diacetylmorphine or Heroin is formed by the acetylization of morphine; the hydrogen atoms of both the phenolic and alcoholic hydroxyl groups are replaced by acetyl groups. Heroin has a similar, but more pronounced action than morphine. Due to its potency and the danger from habit-formation, its manufacture in the United States is forbidden by law and its use has been practically discontinued.

Apomorphine Hydrochloride.—When morphine is treated with hydrochloric acid in a sealed tube, one molecule of water is lost with the formation of apomorphine hydrochloride. Apomorphine decomposes readily and must be rejected if an emerald-green color is produced when it is shaken with distilled water (1 to 100). (See the U. S. Pharmacopœia for structure, tests, etc.)

Apomorphine is an expectorant and an emetic. It is particularly valuable as it may be administered subcutaneously in instances of poisoning. Average dose: expectorant, 1 mg.; emetic, by hypodermic injection, 5 mg.

Papaverine occurs naturally in opium to the extent of about 1 per cent. **Papaverine Hydrochloride** is in white crystals or as a white crystalline powder. It is odorless but has a slightly bitter taste. For other properties and tests of identity see the U. S. Pharmacopœia.

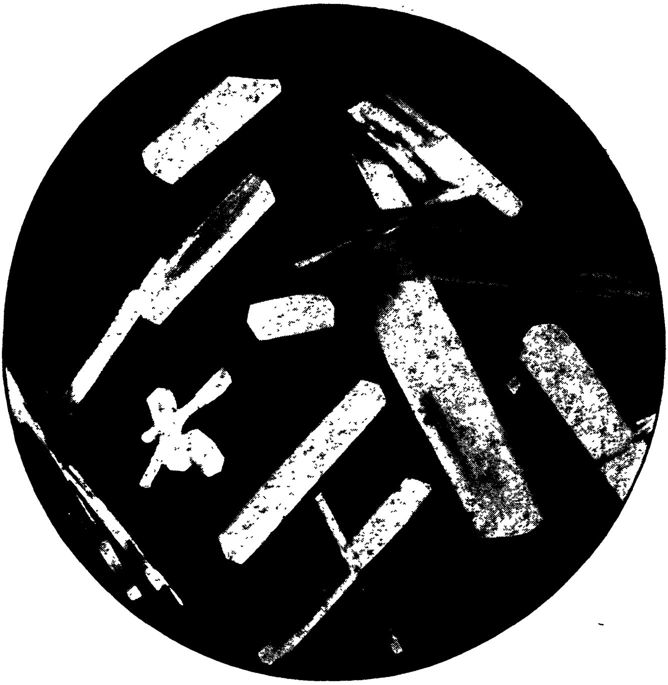


FIG. 151.—Codeine sulfate: orthorhombic crystals from hot alcoholic solution.

Papaverine Hydrochloride is a vasodilator and antispasmodic, and is used particularly in combination with codeine to abort "common colds." Average dose, 60 mg.

Cotarnine Chloride is a yellow, odorless crystalline powder, deliquescent in moist air (see the National Formulary for properties and tests).

It is a uterine and local hemostatic, often sold under the name of **Stypticin.** Average dose, 60 mg.

Dihydromorphinone Hydrochloride, known commercially as **Dilaudid,** differs from morphine hydrochloride in that one of the hydroxyl groups of morphine is replaced by a ketone group and the adjacent double bond is removed. It is prepared by reducing morphine in hydrochloric acid solution with hydrogen in the presence of a catalyst.

The drug is powerfully analgesic and tends to strongly depress the respiratory mechanism. The dosage is smaller than that of morphine; it less frequently causes nausea and constipation than does morphine and perhaps is less habit-forming. Average dose: as a sedative and analgesic 2 mg.; for cough 1 mg.

Narcotine exists in opium as a free base (1.3 to 10 per cent) (see Fig. 152). It possesses no narcotic properties and is therefore sometimes called anarcotine. When hydrolyzed by dilute acids or alkalis it yields opianic acid and hydrocotarnine; upon reduction it yields meconine and hydrocotarnine. When oxidized by boiling with diluted nitric acid it yields cotarnine and opianic acid.

$$\underset{\text{Narcotine}}{C_{22}H_{23}O_7N} + O \rightarrow \underset{\text{Cotarnine}}{C_{12}H_{13}O_3N} + \underset{\text{Opianic acid}}{C_{10}H_{10}O_5}$$

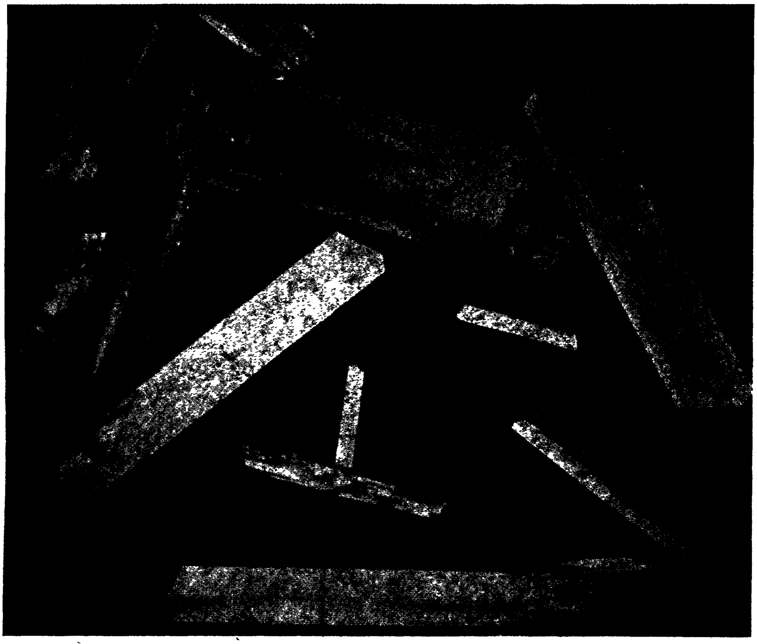


FIG. 152.—Narcotine: orthorhombic crystals from alcoholic solution.

Thebaine is dimethyl morphine. It occurs to the extent of 0.15 to 1 per cent in opium. It crystallizes in prisms which are insoluble in water or alkaline solutions but soluble in alcohol, and give with sulfuric acid a deep red color.

Narceine (0.1 to 0.7 per cent) occurs in silky needles or quadrangular prisms, which are nearly insoluble in cold water and alcohol, and are colored blue with iodine solutions and blood-red with chlorine water and ammonia.

SANGUINARIA

Sanguinaria or Bloodroot (U. S. P. 1820 to 1926; N. F. 1926 to date) is the dried rhizome of *Sanguinaria canadensis* Linné. The generic name is from *sanguinarius*, meaning bloody, and referring to the color of the juice; *canadensis* refers to the plant habitat in Canada. The plant is a low perennial herb (see Fig. 153), with a horizontal branching rhizome bearing slender roots, and containing an orange red latex. The rhizomes are dug during the early summer, deprived of their roots and carefully dried. It grows in rich open woodlands in North America east of the Mississippi, most of the collection taking place in the eastern states. Bloodroot was used by the Indians for staining their faces, and also as an acrid emetic. Its use in home-made cough remedies seems to have been adopted by the early settlers.

Description and Structure.—See Figure 154 and the National Formulary.

Powder.—Sternutatory; taste bitter and persistently acrid; starch grains numerous, 3 to 20 microns in diameter, mostly single, and nearly spheroidal or ovoid, and polarizing light; numerous fragments of parenchyma bearing short laticiferous sacs containing reddish orange, resinous masses; tracheal fragments few, having numerous transverse slit-like pores.

Fig. 153.—A group of transplanted blood root plants (*Sanguinaria canadensis*) showing 1-flowered scapes, and the palmately veined and lobed leaves.

Constituents.—Alkaloids of the protopine series, including sanguinarine, about 1 per cent, chelerythrine, protopine, and *b*- and *g*-homochelidonine; these alkaloids are colorless but tend to form colored salts; sanguinarine, reddish salts with nitric or sulfuric acids; chelerythrine, yellowish salts; protopine is found also in opium and chelidonium, and the homochelidonines in chelidonium. Other constituents include a reddish resin, several organic acids, as citric and malic, and considerable starch. Total ash about 4.75 per cent with about 0.27 per cent of acid-insoluble ash.

All of the alkaloids of sanguinaria are found in other members of the *Papaveraceæ* and, like berberine and hydrastine, are isoquinoline derivatives. While morphine and codeine are not isoquinoline derivatives they can be converted into isoquinoline alkaloids. It is interesting to note that the *Ranunculaceæ*, *Berberidaceæ*, *Menispermaceæ* and *Papaveraceæ* contain alkaloids of this type.

Standards.—Sanguinaria contains not more than 5 per cent of the roots of the plant. Shriveled rhizomes that are gray internally and free from starch should be rejected.

Uses and Dose.—Sanguinaria is a stimulating expectorant and an emetic. Average dose, 125 mg.

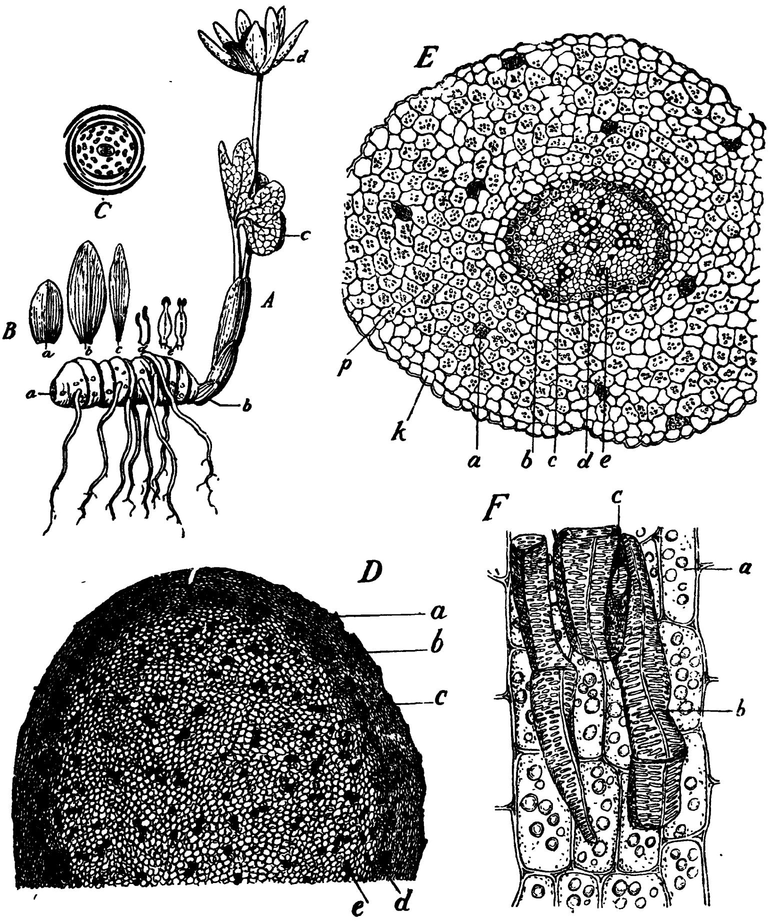


FIG. 154.—Sanguinaria. *A*, entire flowering plant: *a*, rhizome with long rootlets; *b*, one of the outer bud-scales; *c*, young leaf; *d*, the nearly complete flowers, in which the caducous sepals have fallen away. *B*, the separated floral organs: *a*, sepal; *b* and *c*, different petals; *d*, stamens; *e*, pistil in different views. *C*, diagram showing position of parts of the flower. *D*, transverse section of rhizome: *a*, layer of small, thin-walled epidermal cells; *b*, cortex of 10 to 15 rows of thin-walled parenchyma cells containing numerous starch grains, or a small amount of fixed oil; *d*, cambium, most of which is interfascicular, and a narrow circular zone of small collateral fibrovascular bundles, separated from each other by parenchyma; pith large, consisting of starch-bearing parenchyma cells; laticiferous sacs (*c* and *e*) containing a red or orange-colored latex, either isolated or in longitudinal rows and distributed among the parenchymatous cells of the middle bark and pith; sections treated with glycerin show in the secretion cells, after twenty-four hours, spheroidal aggregates of crystals which strongly polarize light. *E*, transverse section of a young root before any important secondary changes have occurred: *k*, layer of epidermal cells; *p*, starch-bearing parenchyma of cortex; *a*, laticiferous sacs; *b*, endodermis; *c*, tracheæ; *d*, pericambium layer, the cells of which are filled with very small starch grains; *e*, leptome. *F*, longitudinal section through tracheal portion of one of the vascular bundles of the rhizome: *a*, starch-bearing parenchyma; *b*, scalariform tracheæ. (After Bastin.)

Chelidonium, or Celandine (U. S. P. 1882 to 1905) is the flowering plant of *Chelidonium majus*, a perennial herb having a milky, orange colored juice, and common in waste places in the northeastern United States and Canada. The drug should be collected at the time of flowering and used in a nearly fresh condition, as the active principles are partially destroyed and diminished on drying.

The powdered dried drug is light green, forming golden-yellow aqueous solutions; it contains seeds composed of nearly cubical thin-walled cells; non-glandular hairs, uniseriate, composed of 6 to 8 long cylindrical cells, some of which are collapsed and somewhat enlarged or swollen at their dividing walls; fragments of leaves with elliptical or spherical stomata on lower surface only, spiral tracheæ, and latex tubes with light yellowish contents; spheroidal pollen grains about 25 microns in diameter, nearly smooth, and having 3 pores; fragments of petals with distinctly yellowish fibrovascular bundles. Starch grains and calcium oxalate crystals are wanting.

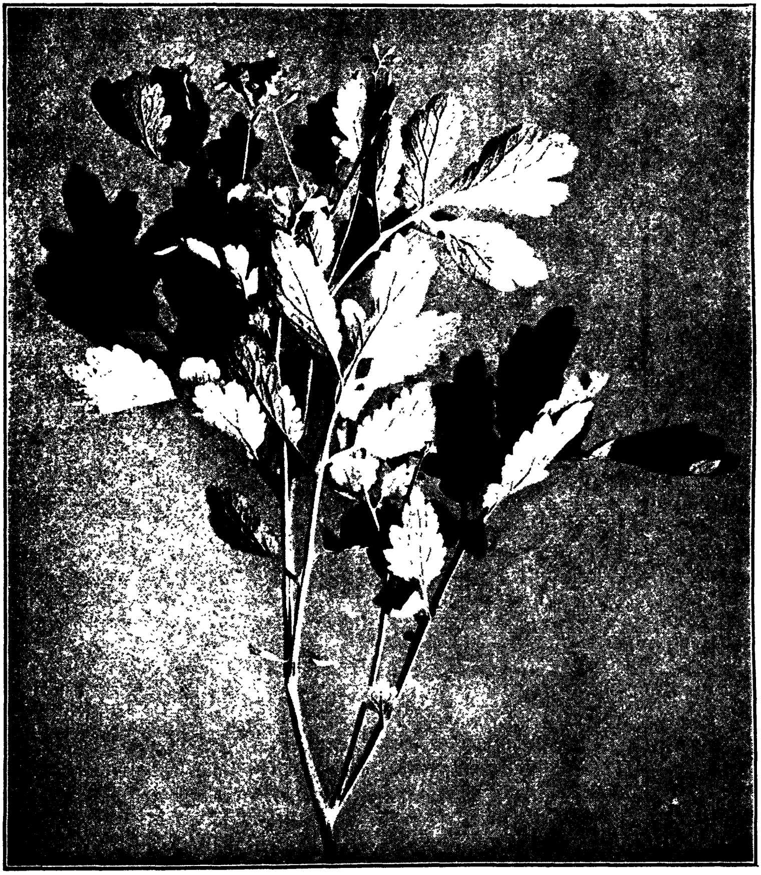


FIG. 155.—Celandine (*Chelidonium majus*), a biennial or perennial herb, with pinnately divided leaves, and terminal clusters of small, yellow flowers. The plant has an orange-colored latex. (After Brown.)

The drug contains 5 or more alkaloids: chelidonine (stylophorine), 0.03 per cent, in colorless monoclinic prisms; chelerythrine, which is fluorescent; α-, β-

and γ-homochelidonine and protopine. These several alkaloids are combined with the following acids: chelidonic, malic, citric and tartaric. It also contains chelidoxanthin, a bitter neutral principle, possessing a yellow color and resembling berberine; and a small quantity of a volatile oil. Another alkaloid, chelilysine, is said to disappear in the drying of the drug. Total ash about 6.5 per cent, with about 0.35 per cent of acid-insoluble ash.

Chelidonium is a sedative, a purgative, also a diuretic, a diaphoretic and expectorant. Average dose, 2 gm.

FUMARIACEÆ, OR FUMITORY FAMILY

This family consists mostly of delicate herbs and a few green shrubs. The leaves are usually compound and the flowers irregular, one or both of the petals having a spurred or a saccate base. The fruit is a unilocular capsule containing one or more seeds. The members of this family are characterized by having special secretion cells termed idioblasts, which are more or less elongated cells, varying from 2 to 10 mm. in length, and occur in the leaves as well as in the axis of the plant.

Corydalis, Turkey Corn, or Squirrel Corn (N. F. 1916 to 1947) consists of the dried tuber of *Dicentra canadensis* (Goldie) Walpers, or of *Dicentra cucullaria* (Linné) Bernhardi. The plants are low, stemless, perennial herbs, common in rich woods in the eastern and central United States and Canada. They have ternately compound and dissected leaves and form racemes of characteristic flowers having heart-shaped spurred corollas, those of *D. canadensis* being tinged with purple, while those of *D. cucullaria* are yellow at the summit.

The tubers of *D. canadensis* are rounded, frequently depressed, and from 5 to 15 mm. in diameter; usually single; externally minutely pitted or nearly smooth, grayish brown or amber-colored and more or less translucent, with a triangular scar on one side and numerous fine roots on the other; fracture either hard and horny (the inner surface being yellowish and waxy), or somewhat tough (the fractured surface being yellowish-white and granular); odor slight; taste bitter.

The bulbils of *D. cucullaria* are the thickened, tuberous bases of the leaves attached to a small upright rhizome, from which they easily separate; they are plump, ovoid or triangular-ovoid, up to 12 mm. in length; externally yellowish or grayish brown, usually translucent; fracture hard and horny, the inner surface being grayish and waxy or granular.

The powder is pale brown to weak yellow; nearly odorless; slightly bitter taste; starch grains numerous, mostly single or 2-compound, from 3 to 60, rarely 90, microns in length, ovoid or oblong; tracheæ few, with simple pores, or reticulate, annular or spiral markings; epidermal cells with thin brownish walls; sclerotic cells irregular in outline, mostly elongated, up to 750 microns long and 150 microns wide with heavily lignified walls about 20 microns in thickness; rosette aggregates of calcium oxalate few and up to 20 microns in diameter.

Corydalis contains several alkaloids, of which protopine (fumarine) and corydaline are the most important; fumaric acid, a yellow bitter principle, resin and starch. Total ash 3 to 4 per cent; acid-insoluble ash, about 0.21 per cent.

Corydalis has been used in the treatment of syphilis. It is said to be tonic and alterative. Average dose, 0.6 gm.

CRUCIFERÆ, OR MUSTARD FAMILY

The plants are mostly herbs, occasionally woody, and include about 200 genera and 2000 species, which are widely distributed. The flowers consist of 4 sepals, 4 petals, 6 tetradynamous stamens and a single compound pistil, becoming in fruit usually a 2-locular silique or silicle. They are especially characterized by their colorless secretion cells located in the parenchyma of the plant. They are stained by the anilin dyes; with solutions of orcin or orcein and hydrochloric acid they are colored violet; with Millon's reagent, the contents are precipitated and colored

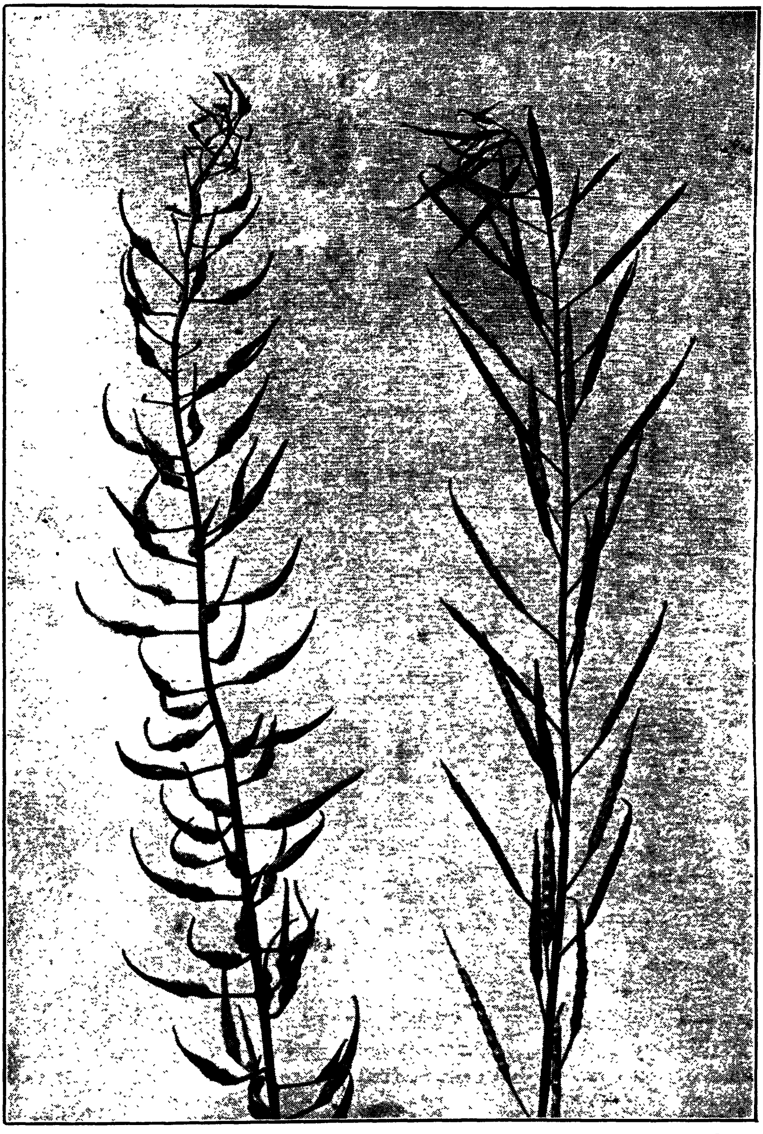


Fig. 156.—Fruiting specimens of the two mustards, the one on the left White Mustard (*Brassica alba*), and the one on the right Black Mustard (*Brassica nigra*). (After Newcomb.)

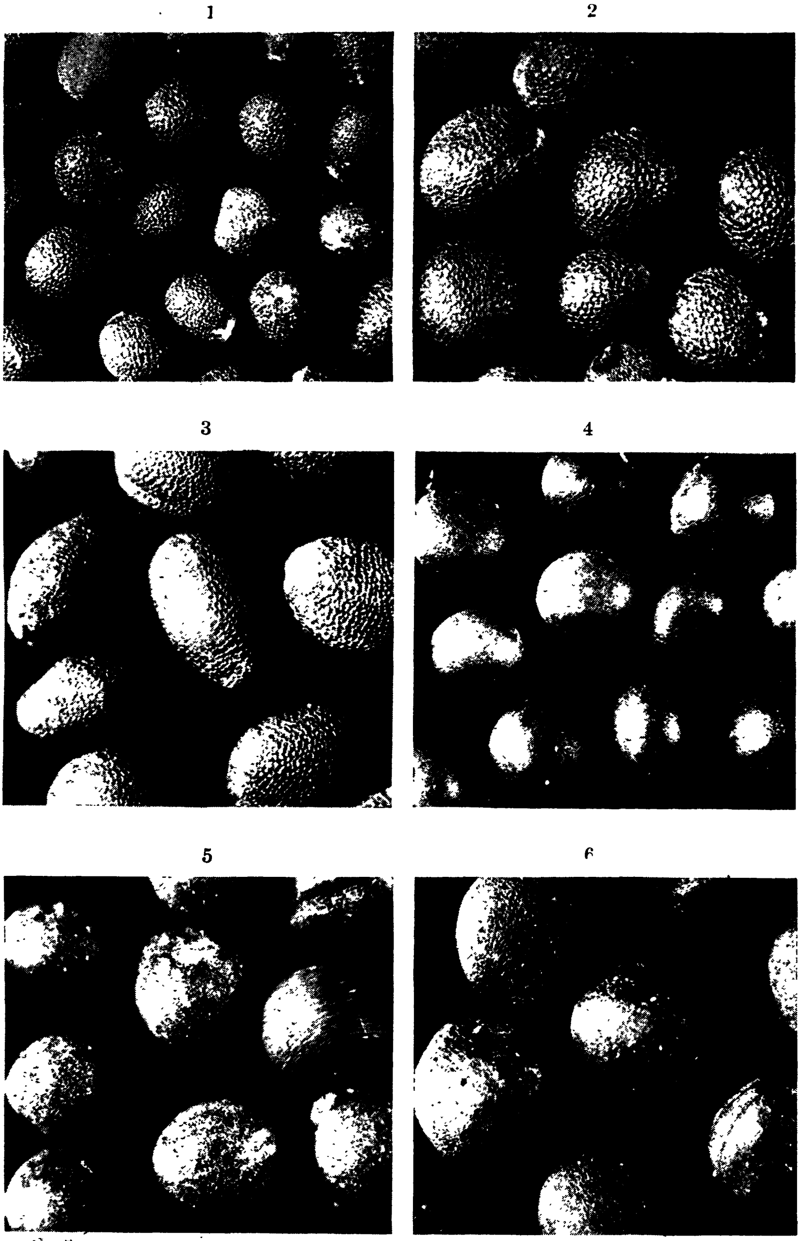


FIG. 157.—Commercial Brown Mustards: *1*, Trieste Mustard (***Brassica nigra***); *2*, Indian Mustard (***B. juncea***); *3*, Sarepta Mustard (***B. besseriana***); *4*, Charlock (***B. arvensis***); *5*, Rape seed (***B. Napus***); *6*, Cabbage seed (***B. oleracea***). (Photos by Paul D. Carpenter.)

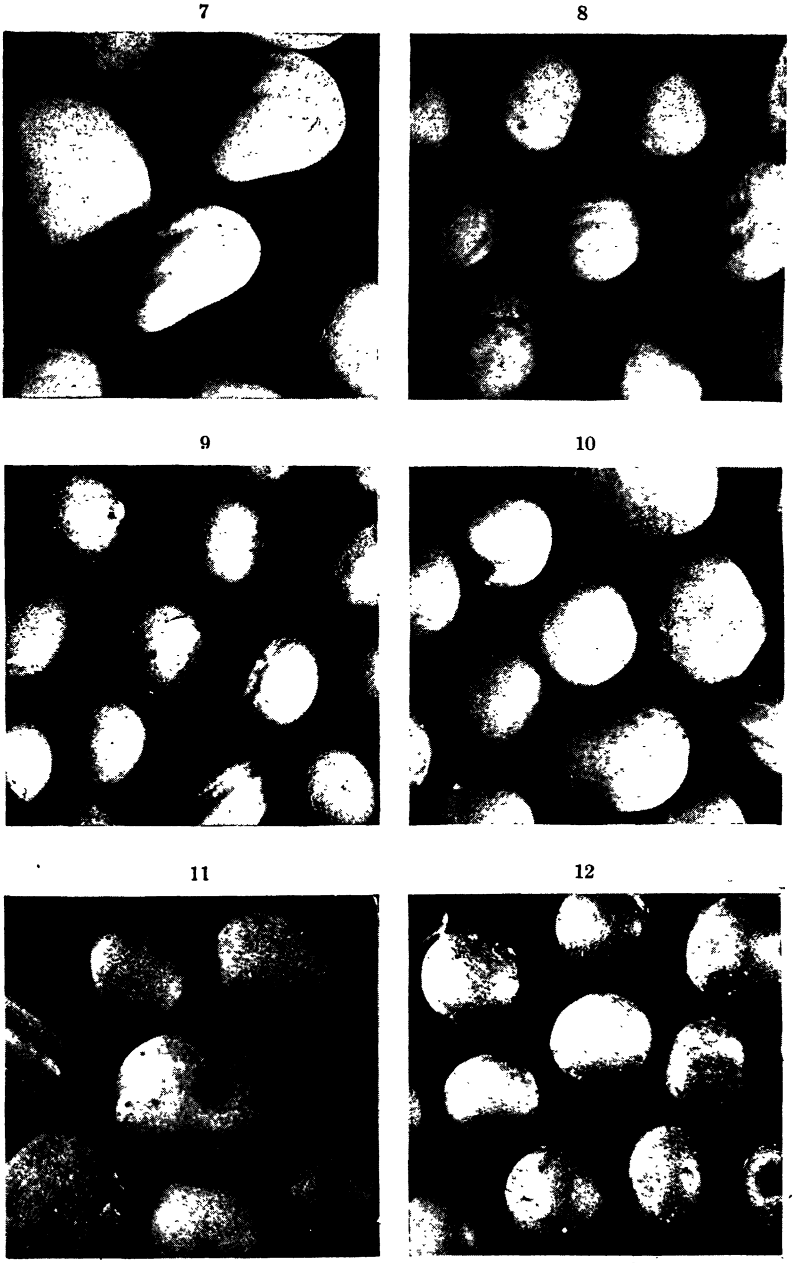


Fig. 158.—Commercial Yellow Mustards: *7*, Indian Colza (*Brassica campestris* var. *sarson*); *8*, Chinese Colza (*Brassica chinensis*); *9*, Japanese Mustard (*Brassica cernua*); *10*, Yellow (White) Mustard (*Brassica alba*); *11*, Indian Tori (*Brassica glauca*); *12*, German Rape (*Brassica rapa*) (No. 12 belongs to the Brown Mustards). (Photos by Paul D. Carpenter.)

red. In alcoholic material the contents of the secretion cells are precipitated and their position more readily determined. Myrosin-secreting cells occur in nearly all of the *Cruciferæ*, with the exception of *Capsella*, *Lepidium*, *Cakile*, and a few others. In the epidermis of the leaves of the *Cruciferæ* occur large water-storage cells readily distinguished by their greater size. The non-glandular hairs are unicellular and of various characteristic shapes for the different genera. Glandular hairs are seldom found, and calcium oxalate is wanting.

MUSTARD

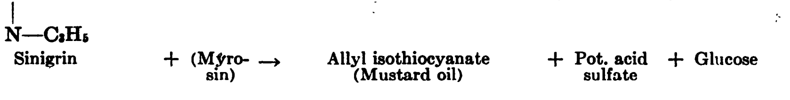
Black Mustard or Brown Mustard (U. S. P. 1820 to date) is the dried ripe seed of *Brassica nigra* (Linné) Koch or of *Brassica juncea* (Linné) Czerniaew or of varieties of these species. The term *Cruciferæ* is from the Latin, meaning cross-bearing, and refers to the shape of the flowers, the petals of which are arranged in the form of a Maltese cross; *sinapis* is from the Celtic *nap*, meaning turnip; *Brassica* is from the Celtic *bresic*, meaning cabbage; *juncea* is Latin, meaning rush or reed; and *nigra* is Latin, meaning black. The term *mustard* is from the Latin *must* and refers to the ancient custom of pounding the seeds with vinegar, then known as *must*.

The plants are annual herbs (see Fig. 156) having slender erect stems, yellow flowers, pinnatifid leaves, and somewhat four-sided siliques with short stalks. They are native to Europe and southwestern Asia but are naturalized and cultivated in temperate climates in many countries, and show considerable variations in form. *B. nigra* is widely cultivated in England and on the Continent and *B. juncea* is cultivated in India. Indian Mustard has been recognized in the U. S. Pharmacopœia only since 1926. Black Mustard is mentioned by Diocletian (300 A.D.) as a condiment and both Theophrastus and Pliny mention its use in medicine. During the Middle Ages it was esteemed as an accompaniment to salted meats. The popularity of mustard as a condiment has by no means diminished today. Besides the home production the United States imports about 15,000,000 pounds annually.

Description and Structure.—See Figures 157, 158, 159 and the U. S. Pharmacopœia.

Powder.—Light olive brown; consisting mostly of tissues of the embryo, the cells containing small aleurone grains and fixed oil, the latter forming in large globules on the addition of chloral T.S.; fragments of the seed coat exhibiting the so-called "shadow effect" are particularly characteristic (see Fig. 159). A portion of the fixed oil is removed by pressure from the crushed seed to facilitate powdering.

Constituents.—Black mustard contains fixed oil (30 to 35 per cent), mucilage and aleurone. Its principal constituent, however, is the glucoside sinigrin (potassium myronate), which is accompanied (probably in adjacent cells) by the enzyme myrosin. Upon the addition of water to the crushed or powdered seeds the myrosin brings about the hydrolysis of the sinigrin as follows:



$$\begin{array}{l} \text{O—SO}_2\text{OK} \\ \;| \\ \text{C—S—C}_6\text{H}_{11}\text{O}_5 + \text{H}_2\text{O} \rightarrow \text{S=C=N—CH}_2\text{—CH=CH}_2 + \text{KHSO}_4 + \text{C}_6\text{H}_{12}\text{O}_6 \\ \;| \\ \text{N—C}_3\text{H}_5 \end{array}$$

Sinigrin + (Myrosin) → Allyl isothiocyanate (Mustard oil) + Pot. acid sulfate + Glucose

The allyl isothiocyanate formed is volatile and may be removed by distillation, the resulting product being the official volatile oil of mustard.

Microchemistry.—A small quantity of powdered black mustard is macerated in water for two hours and then distilled in a microdistillation apparatus: 1 drop of the distillate will give fine needles with phenylhydrazine (base). Dilute the distillate with one-half its volume of ammonia water, allow to stand for a few hours, and permit a drop or so to evaporate on a slide: crystals of thiosinamine are formed which vary considerably, depending upon the concentration

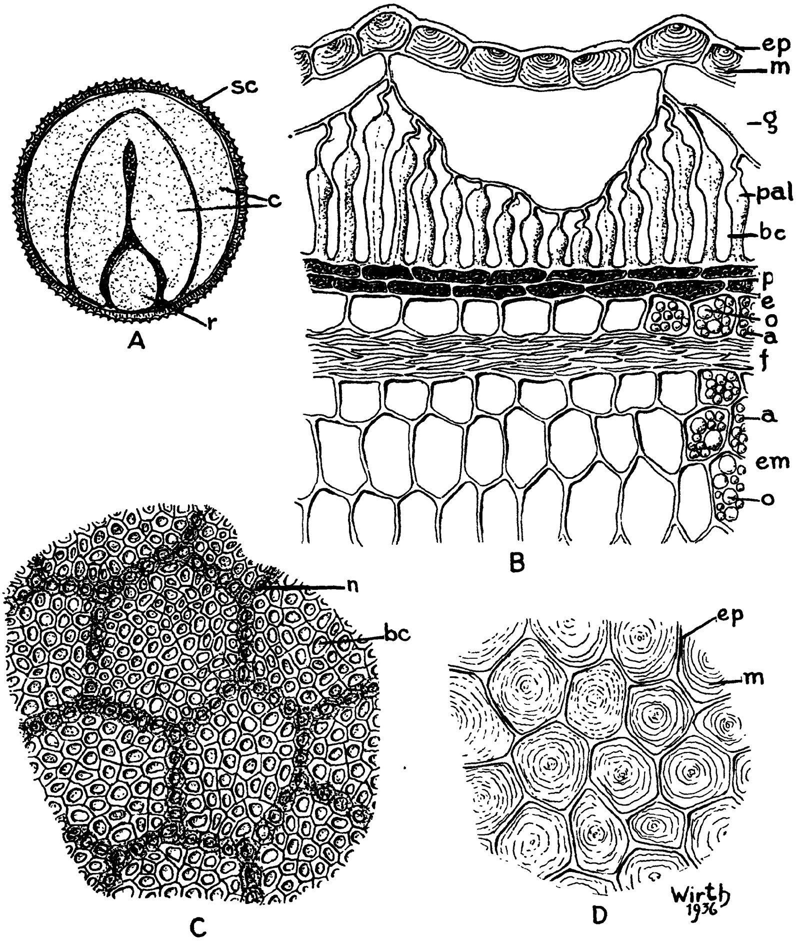
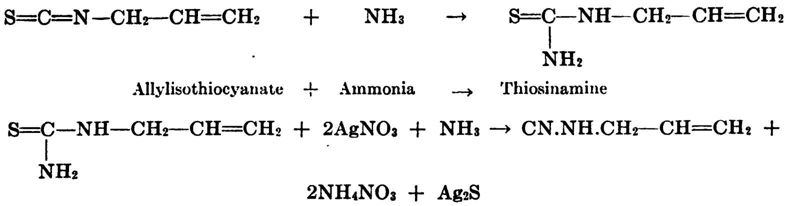


Fig. 159.—Sinapis Nigra. *A*, transverse section through the seed showing seed coat (*sc*), cotyledons (*c*) and radicle (*r*); *B*, transverse section through the outer portion of the seed showing epidermis (*ep*) containing mucilage (*m*), giant cells (*g*), a palisade layer (*pal*) composed of peculiarly thickened stone cells, the so-called "beaker cells" (*bc*) which are of unequal height, a pigment layer (*p*) consisting of one or two rows of cells with brownish contents, a single row of somewhat quadrangular cells (*e*) which contain fixed oil (*o*) and small aleurone grains (*a*), a layer of collapsed cells (*f*), which together with the quadrangular cells (*e*) comprise the endosperm, embryo cells (*em*) with thin walls, fixed oil (*o*) and aleurone (*a*); *C*, surface view of the palisade layer (as seen in the powder) showing the beaker cells (*bc*) the taller of which appear darker and give rise to a shaded network resembling large cells (*n*) (shadow effect); *D*, surface view of the epidermal cells (*ep*) containing mucilage (*m*) which swells in the water mount. (Drawings by Wirth.)

and the presence of impurities. Add a drop of silver nitrate to a drop of the thiosinamine solution: long needles, mostly branching or in bundles or rosettes are formed. The latter reaction is quantitative and is utilized to assay black mustard, the amount of allyl isothiocyanate formed being calculated from the amount of silver nitrate used in reaction. The reaction proceeds as follows:



$$S{=}C{=}N{-}CH_2{-}CH{=}CH_2 \; + \; NH_3 \; \rightarrow \; S{=}\underset{NH_2}{\underset{|}{C}}{-}NH{-}CH_2{-}CH{=}CH_2$$

Allylisothiocyanate + Ammonia → Thiosinamine

$$S{=}\underset{NH_2}{\underset{|}{C}}{-}NH{-}CH_2{-}CH{=}CH_2 + 2AgNO_3 + NH_3 \rightarrow CN.NH.CH_2{-}CH{=}CH_2 + 2NH_4NO_3 + Ag_2S$$

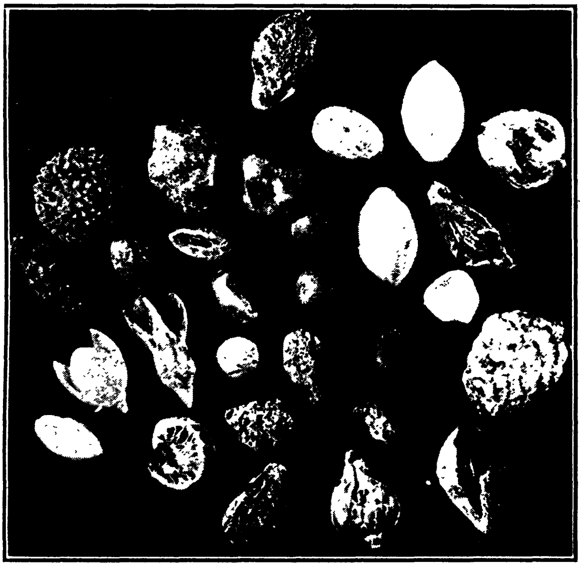


FIG. 160.—A mixture of fruits and seeds picked out from a commercial "Black" Mustard. The mustard is screened out from wheat, particularly in Minnesota and the Dakotas. Eleven different weed seeds or fruits are shown in the picture. (Photo by Paul D. Carpenter.)

The presence of sinigrin (which has an atom of potassium in the molecule) may be demonstrated by the usual microchemical reactions for potassium (platinic chloride, tartaric acid). The reaction is of doubtful value as an identity test for black mustard since potassium from other sources may give the reaction.

STANDARDS.—Black mustard yields not less than 0.6 per cent of volatile oil of mustard (calculated as allyl isothiocyanate). Black mustard contains not more than 5 per cent of other seeds (see Fig. 160) or other foreign organic matter (see Fig. 160).

USES AND DOSE.—Mustard is an emetic and condiment, and is used externally as a rubefacient and a vesicant. Average dose, emetic, 10 gm.

ADULTERANTS AND SUBSTITUTES.—The black mustard of commerce may be admixed with the seeds of **Wild Mustard** or **Charlock** (*Brassica arvensis*). This plant is very common in the wheat fields of the Northwestern States and the seeds are almost always present in the mustard from this territory. A product known as **Dakota Mustard** consists largely of the seeds of this plant. They are very easily detected by the use of a small magnifying glass, as they are brownish black, from 1 to 1.5 mm. in diameter, nearly smooth and not reticulated as are those of true black mustard. Charlock, when admixed with powdered black mustard, can be detected microscopically by the palisade stone cells, which become blood-red on heating with chloral T.S.

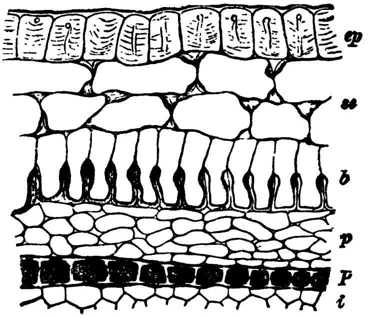


FIG. 161.—Transverse section of White Mustard: *ep*, epidermis; *se*, collenchyma; *b*, palisade layer of stone cells which have the inside and lower portions of the side walls considerably thickened (so-called beaker cells); *p*, several layers of parenchyma; *P*, aleurone cells with thick walls, an oily cytoplasm and numerous very small, somewhat spheroidal aleurone grains; *i*, layer of usually more or less compressed cells, but here shown as being polygonal in outline. (After Moeller.)

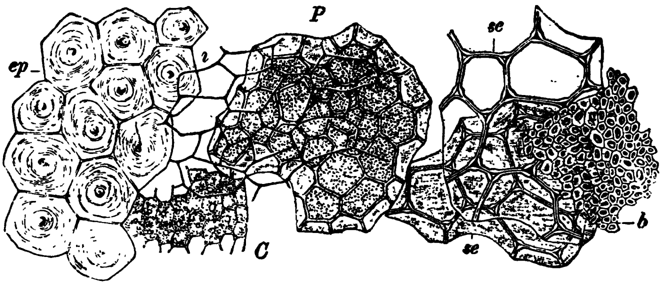


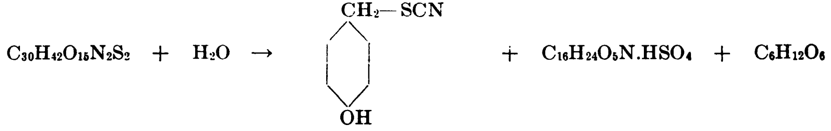
FIG. 162.—White Mustard. Surface view of the different tissues as seen in the powder. *ep*, polygonal cells of the outer epidermis showing mucilage lamellæ and the reduced lumina due to swelling of the lamellæ; *se*, collenchymatous cells beneath the epidermis; *b*, elongated stone cells (so-called beaker cells); *i*, parenchyma cells beneath the stone cells, which are distinguished from the corresponding layer in a number of other seeds by not containing any pigment; *P*, cells of endosperm containing aleurone; *C*, tissue of cotyledon containing aleurone grains and oil. (After Moeller.)

Of the seeds of other *Cruciferæ*, which somewhat resemble black mustard, the following may be mentioned: the seeds of **Sarepta Mustard** (*Brassica besseriana*), which are larger and distinctly reticulate; **Rape** or **Colza** seed (*Brassica Napus*), which are larger, not reticulate, and of a bluish black color; **Turnip** seed, yielded by *Brassica rapa*, which are somewhat larger but less acrid, and are used in India in place of black mustard.

White Mustard, or Sinapis Alba (U. S. P. 1831 to 1926) consists of the dried ripe seeds of *Brassica alba*, forming as important an article of commerce as does black mustard. The plant resembles that of *B. nigra* except that it is usually considerably shorter and the siliques are more rounded and tapering (see Fig. 156). Like black mustard it is cultivated in temperate climates all over the world.

Most of the commercial supplies come from California, Holland and England. The seeds are subglobular, from 1 to 3 mm. in diameter; externally yellow to yellowish brown; minutely pitted, and showing a ridge and 2 grooves on one curved surface. The structure and powder are described in Figures 161 and 162, the essential differences from black mustard being the absence of pigment cells and the absence of the "shadow effect," the beaker cells being of equal height.

White mustard contains 20 to 25 per cent of fixed oil, mucilage, the ferment myrosin and a glucoside sinalbin which upon hydrolysis yields acrinyl isothiocyanate, a pungent tasting but almost odorless oil much less volatile than allyl isothiocyanate.


$C_{30}H_{42}O_{15}N_2S_2$ + H_2O →
CH_2—SCN
OH
+ $C_{16}H_{24}O_5N.HSO_4$ + $C_6H_{12}O_6$

Sinalbin (and myrosin) + Water → Acrinyl isothiocyanate (Para-hydroxy-benzyl-allyl-isothiocyanate) + Sinapin acid sulfate + Glucose

White mustard exhibits the same therapeutic action as black mustard. In the manufacture of condiments it is customary to mix some of the white mustard with the black mustard, it being supposed that the excess of the ferment in white mustard will change the unconverted glucoside in the black mustard into volatile oil of mustard. It is likely, however, that the enhanced quality of the product is due to the pungent and non-volatile character of the oil in white mustard.

A number of yellow or light brown cruciferous seeds have been imported as substitutes for white mustard, notably **Indian Colza** (*B. campestris* var. *sarson*); **Chinese Colza** (*B. chinensis*); **Japanese Mustard** (*B. cernua*) and **Indian Tori** (*B. glauca*) (see Fig. 158).

Mustard Flour consists of the embryonic tissue of either or both black and white mustard, and may or may not contain fixed oil. It is usually prepared by grinding the cake from which the oil has been pressed. The resultant powder is then sifted to remove the "hulls" (seed coats), thus leaving the embryonic tissue together with the cell contents (aleurone, the glucosides and myrosin). Some mustard flours also contain considerable fixed oil. The principal adulterants of mustard flour are: (1) Mustard hulls which enter the product through careless sifting or are purposely added and may be detected by their histological characteristics (beaker cells and "shadow effect"); (2) cereal flours or starches, which may be detected by the iodine test or by the characteristic starch grains; (3) curcuma which is added to color the product and which may be detected by the sulfuric acid-alcohol test or by its microscopic characteristics (see page 182); and (4) capsicum, which is added to increase the pungency and which may be detected by the presence of lignified wavy-walled stone cells (see page 570).

If seed-coat fragments are entirely wanting the presence of either black or white mustard cannot be determined microscopically since the embryonic tissue is similar in both. The presence of each may however be determined microchemically. Black mustard will yield allyl isothiocyanate upon maceration in water which may be determined by the methods outlined on page 300. White mustard contains sinalbin which will give a red color with Millon's reagent, a color reaction which sinigrin does not give. This latter test may be carried out by moistening 0.25 gm. of the mustard flour with water, allowing to stand half an hour and then shaking with petroleum ether. The petroleum ether is filtered through a double filter and allowed to evaporate and the residue then treated with Millon's reagent. If an intensive red color is produced, white mustard is present.

Prepared Mustard, German Mustard, French Mustard or Mustard Paste is composed of a mixture of the powdered mustards or mustard flour with salt, vinegar, and with or without spices or other condiments which do not simulate the color of yellow ground mustard. Calculated free from water, fat, and salt, it contains not more than 24 per cent of carbohydrates (calculated as starch), not more than 12 per cent of crude fiber, not less than 5.6 per cent of nitrogen derived solely from the materials herein named (U. S. Dept. Agric.).

Allyl Isothiocyanate or Volatile Oil of Mustard (U. S. P. 1882 to 1947; N. F. 1947 to date) is the oil obtained by maceration with water and subsequent distillation of the dried ripe seed (free from the fixed oil) of *Brassica nigra* (Linné) Koch or of *Brassica juncea* (Linné) Czerniaew or prepared synthetically.

Volatile oil of mustard is usually prepared from the ground cake from which the fixed oil has been removed by expression. It is also prepared synthetically by the decomposition of allyl iodide with potassium sulfocyanate in alcoholic solution. The National Formulary requires the label to state whether the oil is prepared synthetically or distilled from either of the above-mentioned plants.

DESCRIPTION.—A colorless or pale yellow, strongly refractive liquid having a very pungent, irritating odor, and an acrid taste. *Care should be exercised in smelling this oil and it should be tasted only when highly diluted.* (Consult the National Formulary for characters of the oil.)

STANDARDS.—Volatile oil of mustard yields not less than 93 per cent of allyl isothiocyanate.

USES AND DOSE.—Volatile oil of mustard is generally used externally as a rubefacient or vesicant. Internally it is a gastro-intestinal irritant. Average dose, 0.008 cc.

Cochlearia, or Horseradish Root (U. S. P. 1820 to 1863) is the fresh root of *Cochlearia armoracia*. Horseradish contains sinigrin and myrosin and, after crushing and moistening, yields about 0.06 per cent of a volatile oil containing allyl isothiocyanate. It has been used as a drug in place of mustard, and is extensively used as a condiment.

DROSERACEÆ, OR SUNDEW FAMILY

This is a small family of biennial or perennial herbs including the Venus' fly-trap. The typical genus of the family, *Drosera*, possesses peculiarly stalked glands known as glandular tentacles, which secrete a sticky material by which insects are trapped and then secrete a digestive juice which destroys the insect caught within the rolled up leaf. The dissolved proteins are absorbed by the plant as food.

Drosera, or Sundew (N. F. 1916 to 1936) is the entire plant of *Drosera rotundifolia*, frequently mixed with the closely allied species *D. anglica* and *D. longifolia*, or at times wholly replaced by these. The drug is more or less crumpled and matted; the leaves are petiolate, mostly basal, 7 to 15 mm. in diameter, abruptly narrowed into the petioles and covered with numerous pinkish red glandular tenacles, about 4 mm. in length.

The drug contains a greenish brown resin, having a slight odor and a very acrid taste; an enzyme capable of converting albumin into peptone; also citric acid and probably malic acid. Total ash about 4.25 per cent; acid-insoluble ash about 0.75 per cent.

Drosera is used as a pectoral. It has had some reputation as a remedy for whooping cough. Average dose, 4 gm.

SAXIFRAGACEÆ, OR SAXIFRAGE FAMILY

These are mostly perennial herbs, seldom annual plants or shrubs The family is represented by about 70 genera and 600 species which are mostly indigenous to the North Temperate zone. The fruit are especially characterized by having a small embryo embedded in a large endosperm. The tracheæ always possess scalariform perforations and the walls adjoining the parenchyma are usually marked by simple pores.

Hydrangea, or Seven Barks (N. F. 1916 to 1926) consists of the dried rhizome and roots of *Hydrangea arborescens*. The plant is a beautiful shrub growing wild along the rocky banks of streams throughout the central and southern United States.

The rhizome is cylindrical, usually in pieces 3 to 20 mm. in diameter; light brown to yellowish brown with a pinkish tinge; longitudinally wrinkled and marked by a few elliptical lenticels, occasional prominent buds, short branches or stem-scars, while from the lower surface arise a few coarse fibrous roots; fracture tough, splintery; internally pale yellowish orange; bark thin, easily separable from the distinctly radiate wood.

Hydrangea has a corky layer consisting of several rows of grayish white tabular cells; a cortex consisting chiefly of starch-bearing parenchyma, large cells containing raphides, small isolated groups of stone cells, and sclerenchymatous fibers; a woody cylinder composed of slender wedges made up of prominent tracheæ with reticulate thickenings and tracheids, separated by the starch-bearing medullary rays, which are from 1 to 3 cells wide; a pith of large polygonal cells with prominent simple pores.

The powder is very pale orange in color, inodorous, and with a slightly sweet and acrid taste. It consists mostly of irregular fragments of the wood containing strongly lignified tracheæ, tracheids and medullary ray cells; stone cells 30 to 200 microns in length, strongly lignified; raphides numerous, 50 to 135 microns in length; starch grains mostly simple, ellipsoidal, occasionally with a prominent central cleft, and varying from 2 to 10 microns in diameter.

The drug contains the glucoside hydrangin, about 1 per cent, crystallizing in aggregates, soluble in alcohol and ether, and giving with solutions of the alkalis a blue fluorescence, which immediately disappears on the addition of acids; a volatile oil; resin and starch; probably also a saponin; total ash, about 2.5 per cent; acid-insoluble ash, about 0.25 per cent.

Hydrangea is said to be diuretic and diaphoretic. Average dose, 2 gm.

Heuchera, or Alum Root (U. S. P. 1820 to 1882) is the dried rhizome and roots of *Heuchera americana* Linné. The plant is a low perennial, the heart-shaped leaves mostly radical.

The rhizome may be up to 30 mm. thick and is usually cut transversely into pieces. It is somewhat compressed, knotty and irregular; yellow or light brown in color, and very astringent in taste. The dried drug contains from 10 to 20 per cent of tannin. It is used as an astringent both internally and externally. It has been largely replaced by tannic acid.

HAMAMELIDACEÆ, OR WITCHHAZEL FAMILY

This is a family consisting mostly of subtropical trees or shrubs and represented by 18 genera and 50 species. The non-glandular hairs are either stellate or tufted. Calcium oxalate is excreted either in the form of solitary crystals or rosette aggregates. Tannin-secretion cells are very characteristic in *Hamamelis*. Schizogenous resin canals in *Liquidambar* occur commonly at the margin of the pith and can be traced into the finest branches of the veins of the leaves. In roots they are associated with the development of primary and secondary phloem.

STORAX

Storax or Liquid Storax is obtained from the trunk of *Liquidambar orientalis* Miller, known in commerce as Levant Storax (U. S. P. 1831 to date), or of *Liquidambar Styraciflua* Linné, known in commerce as American Storax (U. S. P. 1926 to date). In the U. S. Pharmacopœia from 1831 to 1863 Styrax is ascribed to *Styrax officinale.* This plant does not yield Levant Storax as is pointed out in the U. S. Dispensatory of 1833.

The term *Styrax* is from the Arabian *asstirax*, meaning a sweet smelling exudation; *Liquidambar* is from the Latin *liquidus,* meaning fluid and the Arabian *ambar,* meaning amber; *orientalis* means pertaining to the Orient and *styraciflua* means to flow storax. *L. orientalis* is a tree attaining the height of about 15 meters and grows in Asia Minor. *L. styraciflua* is a tree attaining a height up to 40 meters and grows in southern North America, Central America and northern South America. Levant storax is a pathological product, its formation being induced by bruising or puncturing the bark of the tree in early summer, which causes the cambium to produce new wood with balsam-secreting ducts. In autumn, the bark which is more or less saturated with balsam, is peeled off and the balsam recovered by pressing. The bark is then boiled in hot water and again pressed. The balsam is poured into casks or cans and is usually exported via Smyrna. Most of the American storax is produced in Honduras where large forests of *L. Styraciflua* are found. The balsam exudes into natural pockets between the bark and the wood which may be located by excrescences on the outside of the bark. These pockets which contain up to 8 pounds of the balsam are tapped with gutters and the balsam led into containers. The balsam is exported in tin cans. A small quantity is also produced in the United States. The early Arabian physicians were acquainted with storax and it is mentioned as early as the twelfth century.

Description.—Levant storax is a viscid, grayish to grayish brown, more or less opaque, semiliquid mass, depositing on standing a heavier, dark brown, oleoresinous stratum. American storax is a nearly clear, yellowish brown semiliquid, becoming hard, opaque and darker colored. Storax is transparent in thin layers; odor agreeable; taste balsamic.

Storax is insoluble in water but almost completely soluble in warm alcohol; it is soluble in ether, carbon disulfide, benzol or acetone but insoluble in benzin.

Constituents.—Levant storax consists of about 50 per cent of two resin alcohols, *α-storesin* and *β-storesin,* which are partly free, partly in combination with cinnamic acid and partly with sodium. α-Storesin is amorphous but forms a crystalline compound with potassium; β-Storesin occurs in white flakes which do not form a crystalline compound with potassium. Styrax also contains storesin cinnamate, 10 to 20 per cent; styracin or cinnamyl cinnamate, 5 to 10 per cent, in needle-crystals that are colorless, odorless and tasteless; phenylpropyl cinnamate, 10 per cent, a liquid with the odor and taste of styrax; volatile oil 0.5 to 1 per cent; a trace of vanillin; free cinnamic acid from 2 to 5 per cent; and small amounts of several other substances. Free cinnamic acid may be obtained from storax by microsublimation (see page 484) with a yield up to 20 per cent.

American Storax contains related storesins and other items found in Levant storax. It yields 7 per cent of volatile oil by steam distillation; and contains about 28 per cent of cinnamic acid, 23 per cent of cinnamein, 35 per cent of resin esters and 2 per cent of resin acids.

STANDARDS.—Storax loses not more than 20 per cent of its weight upon drying at 100° C. for two hours, and not more than 5 per cent of residue remains after thorough extraction with boiling alcohol. The alcoholic solution upon drying yields a yellowish brown residue (not less than 70 per cent of the weight of storax taken) known as **Purified Storax** (U. S. P. 1831 to 1863). Purified storax yields not less than 25 per cent of cinnamic acid, and has an acid value of from 50 to 85 for Levant storax and from 38 to 85 for American storax. Its saponification value is not less than 160 and not more than 200. When the balsam is boiled with a solution of potassium permanganate and sulfuric acid it evolves an odor resembling that of bitter almonds (due to the presence of cinnamic acid); it forms little or no foam when mixed with an equal volume of alcohol and shaken with ammonia water, indicating the absence of turpentine and fixed oils. It should be free from rosin and rosin oils.

USES AND DOSE.—Storax is a stimulant, an expectorant and an antiseptic. Average dose, 1 gm.

Cinnamic Acid ($C_6H_5.CH:CH.COOH$) was first obtained from cinnamon oil by Dumas in 1834. It is now commercially obtained from Peru balsam, Tolu balsam, storax or cinnamon oil, or is produced synthetically from benzaldehyde. It occurs in white crystals and forms salts with alkalis. The acid is readily soluble in alcohol and the usual organic solvents; sodium cinnamate is readily soluble in water.

Cinnamic acid and its salts cause leucocytosis and have been used medicinally for this purpose; also in tuberculosis of the lungs and skin, though the results have not been markedly favorable. As an application to the skin, a 5 per cent alcoholic solution is used; average oral dose, 150 mg.; intravenously, 10 mg.

ADULTERANTS.—Levant storax has been very extensively adulterated with dirt and inorganic materials, other gums, resins and oils, etc. An entirely **factitious storax** has been prepared so as to resemble storax and is still a common article of commerce.

ALLIED PRODUCTS.—Storax is also obtained from *Altingia excelsa,* of the Indian Archipelago. This tree yields a soft, white, crystalline balsam, developing the fragrant odor of styrol and containing about 50 per cent of an ester of cinnamic acid. A brown, solid balsam is also obtained from it. This balsam has an odor of cinnamon and contains a trace of free cinnamic acid and 9.7 per cent of cinnamic acid in the form of an ester. The oil from this plant is known as **Rasamala wood oil,** and contains a ketone.

HAMAMELIS

Hamamelis Leaf or Witch Hazel Leaves (U. S. P. 1882 to 1916; N. F. 1916 to date) is the dried leaf of *Hamamelis virginiana* Linné.

Hamamelis Bark, or Witch Hazel Bark (U. S. P. 1905 to 1916) consists of the bark and twigs of *Hamamelis virginiana.*

Hamamelis is from the Greek *hama,* meaning "at the same time" and *melis* meaning "a fruit;" *virginiana* indicates that the plant is found in Virginia. The plant is a shrub or small tree attaining a height of 8 meters. The flowers appear in the fall at the same time as the ripening fruits from the previous year. The leaves or bark are collected in autumn and carefully dried, commercial supplies coming from Virginia,

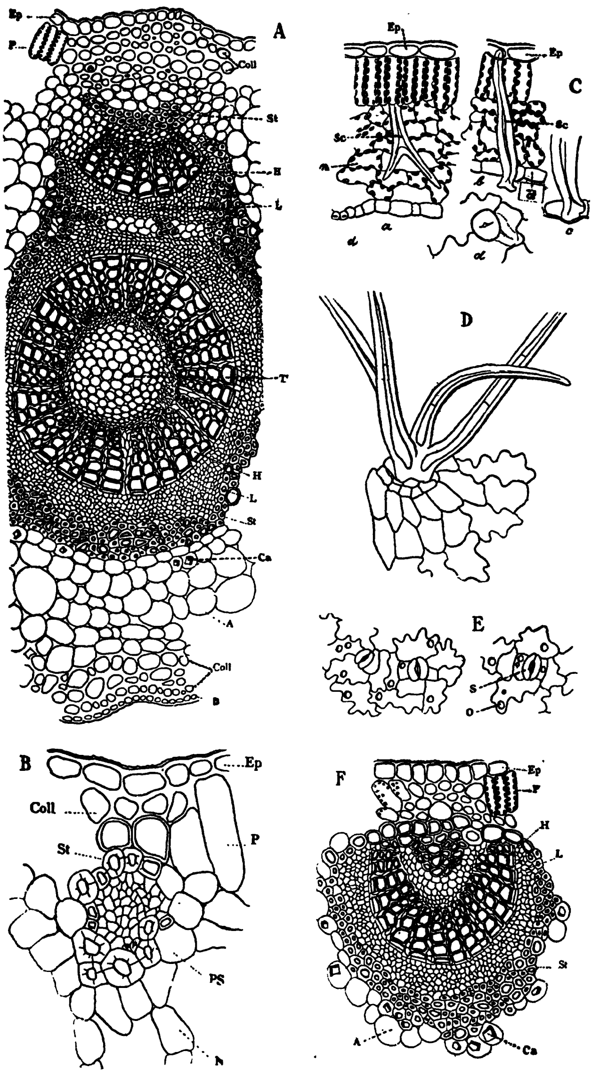


FIG. 163.—Hamamelis Leaf: *A*, transverse section of a midrib from about middle of the leaf-blade, showing an arch-shaped collateral vascular bundle situated near the upper or ventral epidermis and a stele with a central pith (*T*) near the center of the section: *Ep*, ventral epidermis; *Coll*, collenchyma; *P*, palisade cells; *St*, sclerenchymatous fibers; *H*, tracheæ; *L*, sieve; *T*, pith; *Ca*, calcium oxalate; *A*, colorless tissue; *D*, dorsal epidermis. *B*, transverse section of a thin mesotome strand of leaf-blade: *Ep*, ventral epidermis; *Coll*, collenchyma; *P*, palisade tissue; *St*, stone cells; *PS*, parenchyma sheath; *N*, loose mesophyll. *C*, transverse section of leaf-blade: *Ep*, ventral epidermis; *D*, dorsal epidermis; *Sc*, colorless stone cells (also called idioblasts); *N*, loose mesophyll; in figures *a* and *b* the palisade and pneumatic tissue are shown with thick-walled stone cells, branched in *a*, penetrating epidermis in *b*; in *c* one end of a sclereïd is entering an epidermal cell, and in *d*, is shown a surface view of the epidermis with the end of a stone cell. *D*, basal portion of a 4-branched hair from the dorsal epidermis of leaf, showing very thin cross-walls in the branches. *E*, surface view of dorsal epidermis of leaf-blade, showing the stomata (*S*) and oil globules (*O*). *F*, transverse section of a midrib from near the summit of the leaf-blade; letters as *A*. (After Holm.)

Tennessee and South Carolina. The decoction or infusion of witch-hazel leaves has been in common use from the days of the American Indian, whose use of the plant led the early settlers to its employment.

DESCRIPTION AND STRUCTURE.—Leaves and bark: see Figures 163 and 164 and the National Formulary.

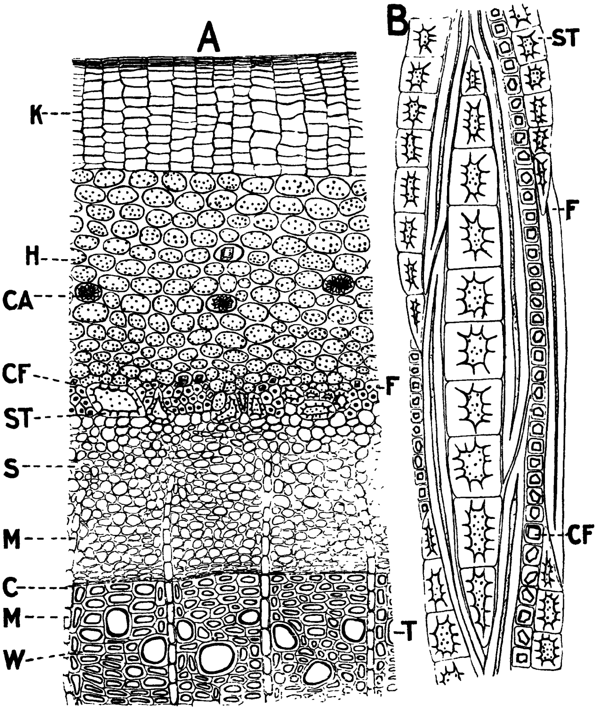


FIG. 164.—Hamamelis Bark: *A*, transverse section of twig: *K*, cork; *H*, cells of cortex with simple pores, the cells containing chloroplasts and small starch grains; *Ca*, calcium oxalate crystals; *Cf*, crystal fibers; *St*, stone cells; *F*, bast fibers with thick, strongly lignified walls; *S*, sieve cells; *M*, medullary rays; *C*, cambium; *W*, wood fibers; *T*, tracheæ. *B*, tangential section of a twig showing stone cells (*St*), crystal fibers (*Cf*), and thick-walled bast fibers (*F*).

POWDER.—The powdered, recently dried leaves are dark green in color; after aging this powder is yellowish brown to light yellow with a slight odor and an astringent, slightly aromatic and bitter taste. The powdered bark exhibits masses of brownish or yellowish cork cells, some of them lignified; groups of parenchyma cells with tannin or small starch grains; strands of lignified bast; tracheæ with bordered pores; strongly lignified wood fibers with slit-like or bordered pores; crystal fibers containing monoclinic prisms of calcium oxalate, the latter up to 40 microns in length. The powdered leaf shows numerous fragments of mesophyll parenchyma associated with epidermis showing numerous elliptical stomata, and non-glandular 1-celled hairs up to 0.500 mm. in length, and arranged in groups of 2 to 15, spreading from the base.

CONSTITUENTS.—Both leaves and bark contain a gallitannin known as hamamelitannin which appears to be derived from gallic acid and a hexose sugar; a volatile oil; a bitter principle; gallic acid and calcium oxalate. **Hama-**

melin is an evaporated alcoholic extract of either the leaves or bark, that of the former being greenish black and more permanent.

Uses and Dose.—Both leaves and bark are astringent and hemostatic. Average dose, 2 gm.

Hamamelis Water or Distilled Extract of Witch Hazel (N. F. 1888 to 1905, 1926 to date; U. S. P. 1905 to 1926) is prepared as follows:

Macerate a weighed amount of the recently cut and partially dried dormant twigs of *Hamamelis virginiana* for about twenty-four hours in about twice their weight of water; then distil until not more than 850 cc. of distillate is obtained for each 1000 gm. of the twigs taken; add 150 cc. of alcohol to each 850 cc. of distillate; mix thoroughly.

Description.—Hamamelis Water is clear and colorless, having a characteristic odor and taste; specific gravity, 0.979 to 0.982 at 25° C.; neutral or slightly acid to litmus paper; and free from *methanol, formaldehyde, acetone* or *isopropyl alcohol.*

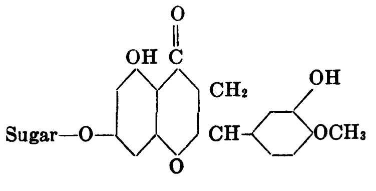
Constituents.—Upon evaporation Hamamelis Water yields not more than 0.025 per cent of dry residue. Alcohol content from 14 to 15 per cent by volume, of C_2H_5OH. The identity of the aromatic volatile principle present is not known; apparently it is not present in the dry witch hazel bark; it may be formed during the maceration of the twigs in the water.

Uses.—Hamamelis Water is applied externally by rubbing or fomentation to relieve congestions, bruises, hemorrhoids, etc.

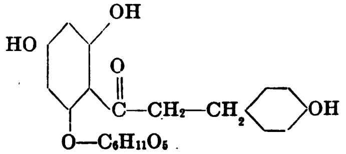
GLYCOSIDES

Glycosides are compounds which upon hydrolysis yield one or more sugars among the products of hydrolysis. The most frequently occurring sugar is β-glucose although rhamnose and other sugars are occasionally found as components of glycosides. Chemically the glycosides are acetals in which the hydroxyl of the sugar is condensed with an hydroxyl group of the non-sugar component and the secondary hydroxyl is condensed within the sugar molecule itself to form an oxide ring. More simply they may be considered as sugar ethers. The non-sugar component is known as the *aglycon.* Using the chemical nature of the aglycon group as a basis of systematization the following classification of the more common glycosides may be devised:

1. **Phenol Group.**—The aglycon groups of many of the naturally occurring glycosides are phenolic in character. Thus *arbutin* (page 478) found in Uva Ursi, Chimaphila and other Ericaceous drugs yields hydroquinone and glucose upon hydrolysis. *Hesperidin* (page 372) occurring in various citrus fruits and *phlorhizin* found in the root bark of various rosaceous plants are phenol glycosides.



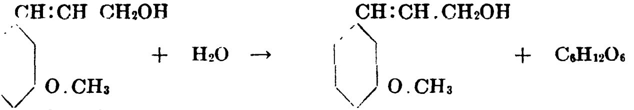
Hesperidin



Phlorhizin

Baptisin (page 358) from Baptisia and *iridin* (page 175) from *Iris* species are additional examples of phenol glycosides.

2. **Alcohol Group.**—*Salicin* whose hydrolysis into saligenin is illustrated on page 202 is an alcohol glycoside. Although saligenin has a phenolic hydroxy group to which the sugar group is attached, the alcohol group classifies it in this category. Together with salicin, another glycoside, *populin* (benzosalicin) (page 202) is found in salicaceous barks. *Coniferin*, a glycoside found in the cambial layer of many pines yields coniferyl alcohol upon hydrolysis.

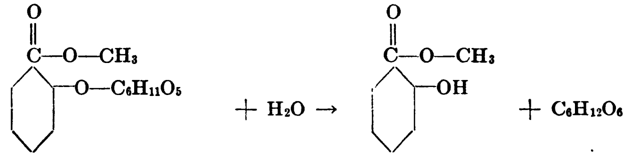


Coniferin Coniferyl alcohol

Coniferyl alcohol (page 188) when oxidized with $K_2Cr_2O_7$ yields vanillin.

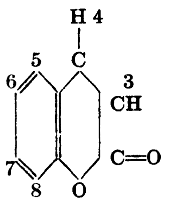
3. **Aldehyde Group.**—*Salinigrin* occurring in *Salix discolor*, consists of glucose combined with *m*-hydroxybenzaldehyde, thus representing a glycoside having an aldehyde aglycon. Salinigrin is an isomer of *helicin* (o-hydroxybenzaldehyde + glucose) and may also be obtained by the mild oxidation of salicin. *Amygdalin* (page 315) which yields benzaldehyde on hydrolysis is still another glycoside that may be classified in this group.

4. **Acid Glycosides.**—Jalap, Ipomœa and Scammony contain glycosides which upon hydrolysis yield resin acids (convolvulinic acid, jalapinolic acid, ipurolic acid). The sugar groups usually consist of rare sugars, d-fucose having been isolated from *jalapin* and d-isorhamnose, a methyl pentose from *convolvulin*. *Gaultherin*, although its aglycon is an ester of salicylic acid, might be classified as an acid glycoside. Gaultherin is found in sweet birch and wintergreen. The sugar present is primeverose.

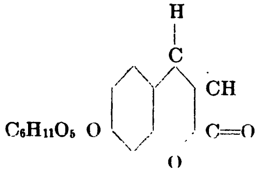


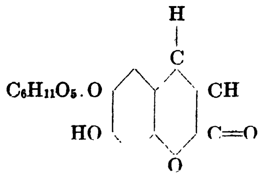
Gaultherin Methyl-salicylate

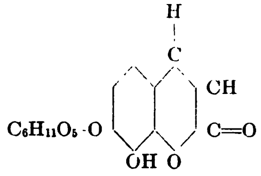
5. **The Oxy-Coumarin Group.**—Although coumarin (page 342) is widely distributed in plants, glycosides containing coumarin as such are rare. Several of its hydroxy derivatives, however, are known. None are of particular medicinal importance but a few occur in certain vegetable drugs. The α-pyrone structure of coumarin may be illustrated as follows for the purpose of discussing these glycosides:

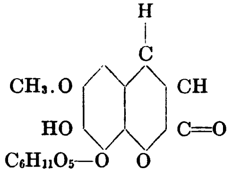


Skimmin occurs in Japanese Star-anise (page 264) and yields upon hydrolysis 7-hydroxy-coumarin or umbelliferone (page 475). *Æsculin* found in the bark of the horse-chestnut tree yields æsculetin, 6,7-dihydroxy-coumarin upon hydrolysis. *Daphnin* found in Mezereum and in *Gnida polycephala* yields daphnetin, 7,8-dihydroxy-coumarin. *Fraxin* found in the bark of several species of ash yields fraxetin, 6-methoxy, 7,8-dihydroxy-coumarin. *Scopolin,* found in Belladonna and in Gelsemium yields scopoletin, 6-methoxy, 7-oxycoumarin. *Limettin* occurring in certain citrus trees is a dimethyl ether of æsculin.

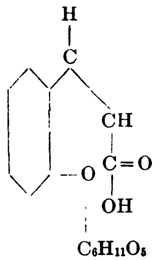

Skimmin


Æsculin


Daphnin


Fraxin

Melilotin from *Melilotus altissima* supposedly yields coumarin itself. Its structure is assumed to be as follows:

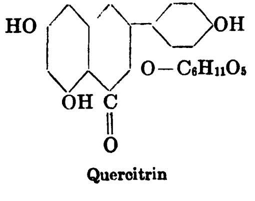


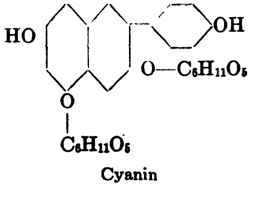
the lactone structure changing to the o-coumarinic acid derivative.

The *Pigment Glycosides* occur between Group 5 and Group 6. Many, if not all, of the red, yellow, violet and blue pigments in plants either exist as glycosides, or are derived from them. In general they may be classified into the three following types:

A. *The Anthraquinones,* such as *alizarin,* from madder root.

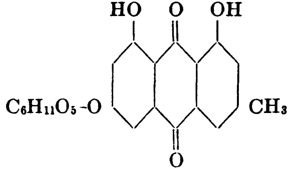
B. *The Flavones or Xanthones.*—Most of the yellow pigments found in plants are flavones such as *chrysin* (5,7-dihydroxy-flavone) from poplar bud, *apigenin* (5,7,4′-trihydroxy-flavone) from celery and parsley, *luteolin* (5,7,3′,4′-tetrahydroxy-flavone) from *Reseda luteola* and *Genista tinctoria* and *quercetin* (3,5,7,3′,4′-pentahydroxy-flavone) from *Quercus tinctorius,* the horse-chestnut, hops, etc.


Quercitrin


Cyanin

C. *The Anthocyanins and Anthoxanthins,* which include most of the red, blue and violet pigments found in plants. Belonging to this group are *cyanin,* the blue pigment in the petals of *Centauria cyanus, idain* from cranberries, *pelargonin* from asters, dahlias and geraniums, *peonin* from peonies, *oenin* from blue grapes, *myrtillin* from the whortleberry, *delphinin* from delphiniums, and so on.

6. **The Anthraquinone Group.**—Closely related to Group A above are a number of glycosides occurring in such drugs as rhubarb, senna, frangula, cascara sagrada, aloe, rhamnus cathartica and rumex. The aglycons of these glycosides are usually di-, tri- or tetra-hydroxymethylanthraquinones (pages 158, 230, 414, 416 and 418). *Frangulin,* yielding frangula emodin (trihydroxy methylanthraquinone) is a typical example.



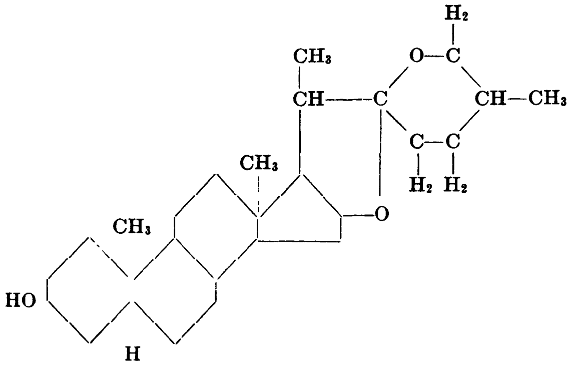
Frangulin

These compounds give the Bornträger reaction (page 159) and may or may not account for the laxative action of these drugs. They are closely related to some of the red and yellow coloring matters found in plants. Ruberythric acid, for example, found in the madder root (*Rubia tinctorum*) consists of two molecules of glucose combined with one molecule of dihydroxymethylanthraquinone. The aglycon of this glycoside is alizarin and was one of the first organic dyes to be synthesized.

7. **The Cyanophore Group.**—Several glycosides yielding hydrocyanic acids as one of the products of hydrolysis are commonly found in rosaceous plants. They are sometimes designated as cyanogenetic glycosides, but since they do not actually produce cyanogen compounds but only liberate them when hydrolyzed, the term "cyanophore" seems to more correctly indicate their properties. The common cyanophore glycosides are derivatives of mandelonitrile (benzaldehyde-cyanhydrin). The group is represented by *amygdalin* (page 315) occurring in bitter almond and *prunasin* occurring in *Prunus padus,* both of which have d-mandelonitrile as the aglycon; *prulaurasin* from cherry laurel leaves having racemic mandelonitrile as the aglycon and *sambunigrin* from *Sambucus niger* having l-mandelonitrile as its aglycon.

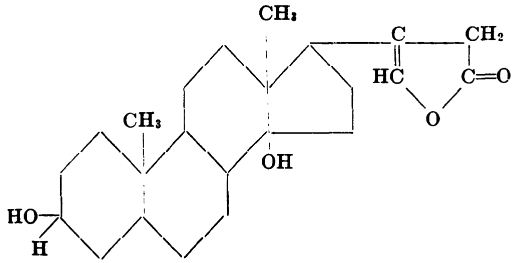
8. **The Thiocyanate Group.**—The seeds of several cruciferous plants contain glycosides, the aglycons of which are thiocyanates. When hydrolyzed by the enzyme "myrosin" they yield the mustard oils. Principal among these glycosides are *sinigrin* from black mustard (page 300); *sinalbin* from white mustard (page 302) and *gluconapin* from rape seed.

9. **The Saponins.**—This group of glycosides is widely distributed in the higher plants. Saponins are characterized by forming colloidal solutions in water which foam upon shaking; they have a bitter, acrid taste and drugs containing them are usually sternutatory and otherwise irritating to the mucus membrane; they destroy red blood corpuscles by hemolysis and they are toxic, especially to cold blooded animals, many having been used as fish-poisons. Upon hydrolysis they yield an aglycon known as a "sapogenin." The sapogenins form readily crystallizable compounds upon acetylization by which means they may be purified and studied. The more poisonous saponins are often called "sapotoxins." Quillaja, Senega and Sarsaparilla are among the more important drugs containing saponins and plants such as may be represented by the California soap plant (*Chlorogalum pomeridianum*) which yields amolonin, are sources of saponins used extensively for industrial purposes.

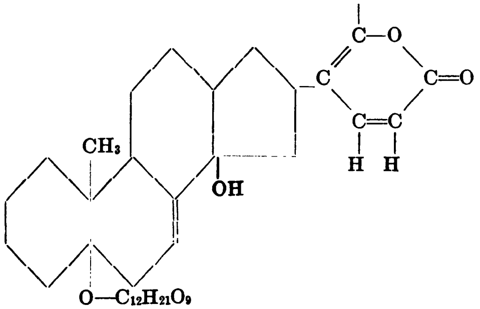


Sarsapogenin

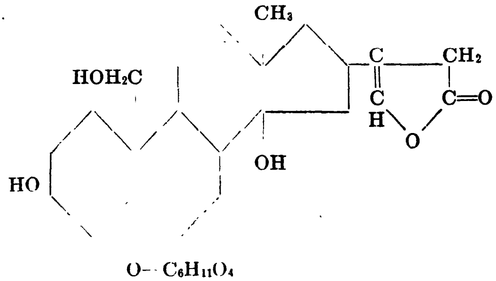
10. **The Cardiac Glycosides.**—The members of this group are characterized by their highly specific action on cardiac and arterial muscle, increasing tone, excitability and contractility. The group includes *digitoxin* and *digitalin* from Digitalis, the *lanatosides* from *Digitalis lanata, strophanthin* and *ouabain* from *Strophanthus* species, the *scillarens* from Squill, *cymarin* from Apocynum, *convallotoxin* from Convallaria and glycosides from Adonis. The aglycons of the cardiac glycosides are often designated as "genins." During the past few years these genins have been the subject of considerable study and much has been learned regarding their chemical constitution. Stereochemical configuration markedly influences the physiological activity of these compounds.



Digitoxigenin



Scillaren A



Ouabain

The ten groups of glycosides discussed above illustrate the wide distribution of this class of compounds in plants. The classification is, however, by no means complete since it is quite possible to find compounds belonging to all classes of organic compounds, combined with glucose or other sugars, in the plant kingdom.

Some glycosides contain more than one saccharide group, possibly as di- or trisaccharides. Upon proper conditions of hydrolysis, one or more of the saccharide groups can be removed from such compounds, resulting in glycosides of simpler structure (see amygdalin below). The most common sugar present is d-glucose although the presence of other sugars such as rhamnose is quite possible. Occasionally rare sugars are found as components of glycosides, such as digitoxose, digitalose and cymarose.

All natural glycosides are hydrolyzed into a sugar and another organic compound by boiling with mineral acids, although they vary widely in the ease with which this hydrolysis is brought about. In most cases, the glycoside is easily hydrolyzed by an enzyme which occurs in the same plant tissue, but in different cells than those which contain the glycoside. Injury to the tissues, the germination process, and perhaps other physiological activities of the cells, result in bringing the enzyme in contact with the glycoside and the hydrolysis of the latter takes place. A large number of enzymes (see page 689) have been found in plants, many of which hydrolyze only a single glycoside; however, two enzymes, namely **emulsin** of almond kernels, and **myrosin** of black mustard seeds, each hydrolyze a considerable number of glycosides. Glycosides which are derivatives of rhamnose require a special enzyme, known as rhamnase for their hydrolysis.

Drugs containing glycosides which liberate the physiologically active constituent only upon hydrolysis, and do not contain it in the free state are sometimes known as "Reactionary Drugs."

ROSACEÆ, OR ROSE FAMILY

This is a family of about 90 genera and 2000 species of great diversity of form. With the exception of the flowers, there are no constant morphological characteristics. The flowers are regular and with numerous stamens. In the woody species the pericycle is composed of either isolated groups of bast fibers, or of a complete and continuous sclerenchymatous ring.

Calcium oxalate occurs in the form of solitary crystals or rosette aggregates, and, with the exception of *Quillaja,* styloids are not present. The secretion cells contain either tannin or mucilage. Lysigenous mucilage canals have been found only in *Neurada.* Gummosis of the parenchyma cells of the cortex and wood is characteristic of many of the species of *Prunus*. The gum exudes spontaneously through rifts or channels in the bark as the result of the pressure of the gum, and collects upon the outer surface in the form of irregular tears. Both glandular and non-glandular hairs are very common to the epidermal tissues of the plants of this family.

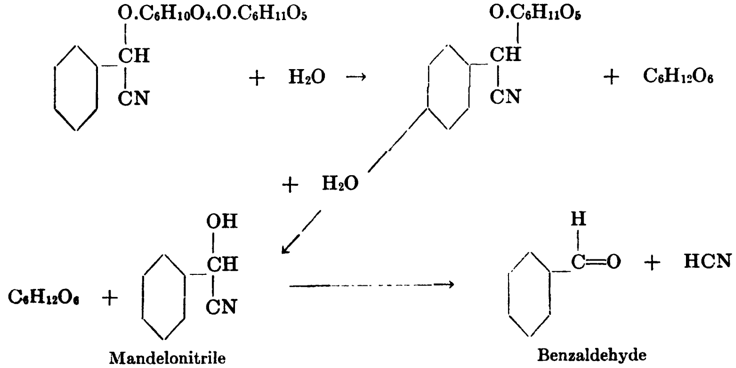
The occurrence of cyanophore glucosides in this family is noteworthy.

The Cyanophore Glucosides

Several glucosides which yield hydrocyanic acid as one of the products of their hydrolysis are found to occur in plants. Perhaps the most widely distributed of these is **amygdalin.** (It will also be noted that another of the products of the hydrolysis is benzaldehyde, and amygdalin may also be classified in the group of aldehyde glucosides.) Amygdalin is found in large quantities in bitter almonds and in the kernels of apricots, cherries, peaches and plums; in the seeds of apples, and practically all seeds of the *Rosaceæ.*

Amygdalin contains two monosaccharide sugar groups; that is, for each molecule of amygdalin, 2 molecules of glucose are formed in the hydrolysis. While these are usually written as linked in apparent disaccharide form, it is particularly noteworthy that it has never been possible to break off a disaccharide sugar from the molecule by any known means of hydrolysis. Amygdalin is therefore a true glucoside rather than a maltoside. The hydrolysis of amygdalin takes place in three steps, which are briefly as follows:

1. Most hydrolyzing agents break the molecule first so as to liberate one molecule of glucose and one of mandelonitrile glucoside.
2. In the next step the second molecule of glucose is liberated with the formation of benzaldehyde-cyanhydrin known as **mandelonitrile.**
3. The mandelonitrile then breaks down with the formation of benzaldehyde and hydrocyanic acid.



The enzyme **emulsin** as obtained from almond kernels consists of a mixture of two enzymes, amygdalase which causes the first step in the hydrolysis and prunase which causes the second step. Besides amygdalin, mandelonitrile glucosides are found occurring in Nature. Three such have been isolated, *i. e.*, *d*-mandelonitrile glucoside, *l*-mandelonitrile glucoside and the racemic *d-l*-mandelonitrile glucoside.

The demonstration of the cyanophore glucosides by **microchemical reactions** in vegetable drugs depends upon their hydrolysis to hydrocyanic acid. Three such reactions might be mentioned as follows:

1. Place a fairly thick section of the drug in 5 per cent alcoholic potash for about a minute. Transfer it to an aqueous solution containing 2.5 per cent ferrous sulfate and 1 per cent ferric chloride and keep at 60° to 70° C. for about

ten minutes. Transfer to 20 per cent hydrochloric acid. The presence of hydrocyanic acid is indicated by the formation of Prussian blue.

2. The reduction of mercurous nitrate (3 per cent aqueous solution) to metallic mercury by hydrocyanic acid has been utilized in localization studies, the presence of hydrocyanic acid being identified by an almost immediate precipitation of black metallic mercury in the cells, the reaction taking place in the cold.

3. The reaction with sodium picrate paper (Guignard Reaction) is carried out as follows: dip strips of white filter paper into a 1 per cent aqueous solution of picric acid; drain and then dip into a 10 per cent solution of sodium carbonate and drain. Place the bruised and moistened plant material in a small Erlenmeyer flask and suspend a strip of the prepared sodium picrate paper above the material, trapping it with a cork. Set aside in a warm place. As soon as hydrocyanic acid is liberated the sodium picrate paper will turn from yellow to brick red or maroon due to the formation of sodium isopurpurate.

Cyanophore glucosides may also be detected in drugs as follows: Saturate pieces of filter paper in a freshly made solution of guaiac resin in absolute alcohol and allow to dry. Moisten a piece of the paper with a very dilute solution of copper sulfate and bring it into contact with a freshly exposed surface of the drug. If hydrocyanic acid is formed a blue stain appears on the paper.

ALMOND

Sweet Almond (U. S. P. 1820 to 1926) and **Bitter Almond** (U. S. P. 1820 to 1916) consist of the ripe seed of *Amygdalus communis* Linné. This plant has been recognized in the U. S. Pharmacopœia as *A. communis* Linné, 1820 to 1842 and 1926 to 1947; as *A. communis* L. var. *dulcis* DC. and var. *amara* DC., 1842 to 1916; as *Prunus amygdalus dulcis* DC., 1916 to 1926, and as *Prunus amygdalus* Batsch, 1947 to date.

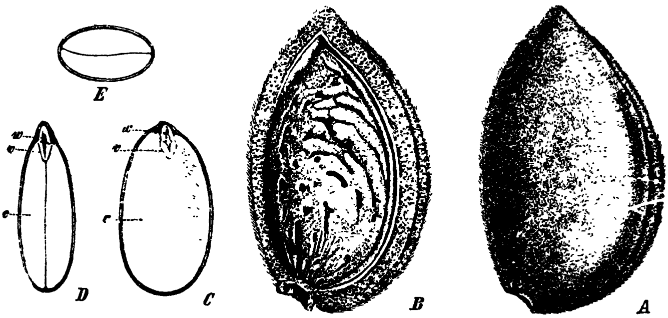


Fig. 165.—Drupe-like fruit of Almond (*Amygdalus communis*): *A*, whole fruit with distinct suture; *B*, longitudinal section showing fibrous sarcocarp, and thin-shelled endocarp; *C*, *D*, *E*, sections of the seed; *c*, cotyledons; *w*, hypocotyl; *v*, epicotyl or plumule. (After Focke.)

Amygdalus is from the Greek *amygdolos*, meaning almond tree; *communis* is Latin meaning common; *amara* and *dulcis* are Latin meaning bitter and sweet, respectively.

The tree is native to Asia Minor, Persia and Syria, and is cultivated and naturalized in all tropical and warm-tempered regions. The presence of amygdalin in the bitter almond and the bitter taste, distinguish it from sweet almond. Commercial products are obtained mostly from Sicily, southern Italy, southern France, northern Africa and California. In commerce the yellowish, more or less porous, fibrous and brittle endocarp may be present (Fig. 165).

Both bitter and sweet almonds are expressed for their fixed oil; bitter almond, after maceration with water, yields a volatile oil of importance in medicine.

Sweet almonds are extensively used as a food, but bitter almonds are not suitable for this purpose. The seeds of the bitter almond were known to be poisonous in the days of antiquity. The sweet almond is mentioned early in the Old Testament (Genesis 43:11), being one of the fruits Israel commanded his sons to carry from Palestine as a gift to Egypt. Theophrastus makes several references to the almond. Charlemagne (812 A.D.) introduced the tree on the imperial farms and in the fourteenth century the almond was an important item of Venetian trade.

DESCRIPTION.—Anatropous, ovate or oblong-lanceolate, flattened, more rounded on one margin, 20 to 30 mm. in length; the bitter almond smaller than the average sweet almond; externally brown; seed coat thin, membranaceous, easily removed after soaking the seed in water; fracture short; without reserve layers; the embryo straight, whitish; hypocotyl, conical, 2 to 3 mm. in length, cotyledons plano-convex, plumule 1 mm. in length; odorless, except on treatment of the bitter almond with water, when odor of hydrocyanic acid is emitted or, if the seeds have been kept for some time, the odor is of benzaldehyde; taste of the bitter almond, bitter; of the sweet almond, bland and sweet.

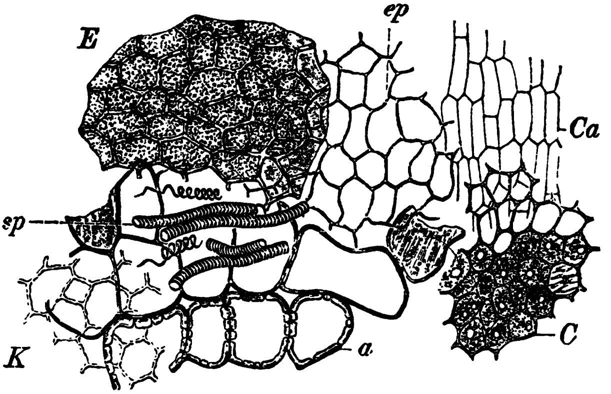


FIG. 166.—Almond Meal: *a*, stone cells of the outer epidermis; *K*, brown hypodermal cells; *sp*, spiral tracheæ of the seed coat; *ep*, cells of inner epidermis which contain a brownish content that is not shown here; *E*, cells of the endosperm containing numerous small aleurone grains; *Ca*, epidermal cells of cotyledons; *C*, parenchyma of the cotyledons containing aleurone grains and oil. (After Moeller.)

STRUCTURE.—In both bitter almond and sweet almond the outer epidermal layer of the seed coat is composed of characteristic, rectangular, somewhat rounded stone cells (see Fig. 167). The cells of the embryo contain numerous aleurone grains, from 5 to 15 microns in diameter, and consisting of crystalloids, globoids and calcium oxalate.

Almond Meal is prepared by grinding **Almond Cake,** the residue left in the press after removing the fixed oil. It is yellowish white in color and contains numerous fragments of parenchyma, containing some oil globules and aleurone grains; also occasional fragments of seed coat. Few or no starch grains are present. The almond meal used as a cosmetic is perfumed especially with orris root. A spurious almond meal consists of wheat middlings to which powdered soap and perfume are added.

CONSTITUENTS.—Bitter almond contains fixed oil, 45 per cent; proteins, 25 to 30 per cent; a glucoside, amygdalin, 1 to 3 per cent; and a ferment, emulsin, which in the presence of water acts upon amygdalin, decomposing it into a volatile oil (benzaldehyde and hydrocyanic acid). In addition to the protein emulsin, there is another casein-like protein present, amandin. Both of these act as emulsifying agents in the preparation of emulsion of almonds. Sweet almond contains no amygdalin, hence does not produce the volatile oil. The yield of fixed oil is usually greater than that from bitter almond.

Amygdalin, or a similar principle is found in the young shoots and flower-buds, as well as the seeds of almond, apricot, peach, plum, cherry and cherry laurel. It is separated from bitter almond and occurs commercially as white, slightly bitter crystals, readily soluble in water and in boiling alcohol, insoluble in ether and but slightly soluble in cold alcohol. It has had some use in medicine in place of hydrocyanic acid.

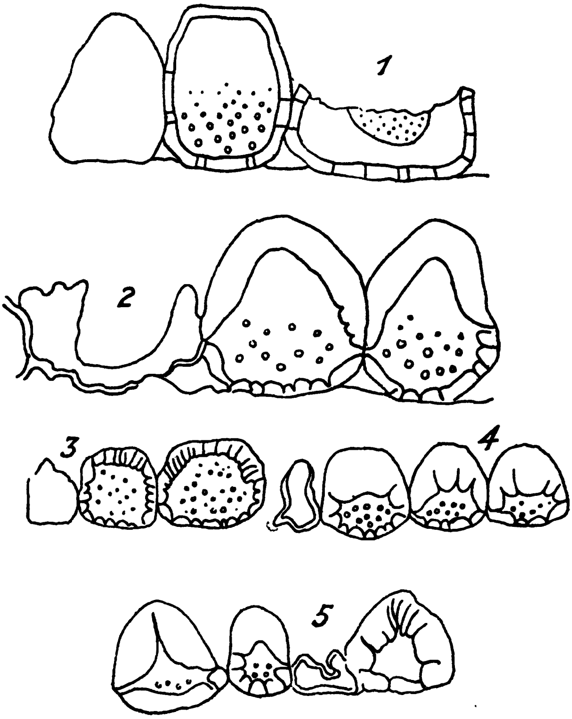


FIG. 167.—Epidermal cells of the seed coat of: *1*, almond; *2*, peach; *3*, apricot; *4*, plum *5*, prune. (After Hanning.)

USES.—Sweet almond is a nutrient and a demulcent. Bitter almond is used as a sedative; it is also a demulcent. Sweet almonds are used as a food, but bitter almonds are poisonous and are used only for the recovery of the oils.

ADULTERANTS.—The seeds of other plants of the *Rosaceæ* are sometimes substituted for almond seeds. These usually have a bitter and more or less disagreeable taste. The outer epidermal cells in apricot and plum are tangentially elongated, while those of peach are somewhat narrower and more or less conical. For the distinguishing characteristics of these and other seed coats, consult Figure 167.

Expressed Almond Oil or Oil of Sweet Almond (U. S. P. 1820 to date) is the fixed oil obtained from the kernels of varieties of *Prunus Amygdalus* Batsch.

The kernels are ground, placed in canvas bags and subjected to a pressure of two to three tons. The expressed oil is allowed to settle, then decanted and filtered. The commercial supply is obtained from bitter almonds prior to maceration for distillation of the volatile oil, and from sweet almonds of inferior quality.

Description, Constants and Tests.—Consult the U. S. Pharmacopœia. The oil should be free from peach kernel oil, apricot kernel oil, sesame oil, cottonseed oil, olive oil, lard oil, paraffin oil and other fixed oils.

Uses.—Expressed Oil of Almond is an emollient, a demulcent and a nutrient.

Persic Oil, Apricot Kernel Oil, or Peach Kernel Oil (U. S. P. 1938 to date) is the oil expressed from the kernels of varieties of *Prunus Armeniaca* Linné or from the kernels of varieties of *Prunus Persica* Sieb. et Zucc.

Persic Oil is prepared in the same manner as expressed almond oil. Its characteristics closely resemble those of expressed almond oil and it is used for the same purposes as this oil.

Bitter Almond Oil (U. S. P. 1851 to 1947; N. F. 1947 to date) is the volatile oil obtained from the dried ripe kernels (deprived of fixed oil) of *Amygdalus communis* Linné, or from other kernels containing amygdalin, by maceration with water and subsequent distillation with steam.

Description and Tests of Identity and Purity.—See the National Formulary.

Standards.—Oil of Bitter Almond contains not less than 80 per cent of benzaldehyde and not less than 2 per cent and not more than 4 per cent of hydrogen cyanide. Oil in which crystals have formed must not be dispensed. Such crystals consist of benzoic acid and are formed by the oxidation of the benzaldehyde.

Uses and Dose.—This drug is a sedative and is so used in cough remedies. Neither it nor its solution should be used or sold for flavoring foods, because of the presence of hydrocyanic acid. Average dose, 0.03 cc.

Benzaldehyde (U. S. P. 1905 to 1936; N. F. 1936 to date) contains not less than 98 per cent of C_6H_5CHO. It is prepared from bitter almond oil or from chlorinated toluene.

Description, Constants and Tests.—See the National Formulary. Benzaldehyde must be free from hydrocyanic acid, chlorinated compounds and nitrobenzene.

Uses and Dose.—Benzaldehyde is used as an antispasmodic and an anesthetic; commercially, as a flavoring in foods, pharmaceuticals and perfumery. Average dose, 0.03 cc.

Diluted Hydrocyanic Acid or Prussic Acid (U. S. P. 1820 to 1926; N. F. 1936 to 1947) is a 2 per cent aqueous solution of HCN.

It is a colorless liquid with the odor of bitter almond oil. It is miscible with water and with alcohol. It gradually decomposes, turning brown, and should be kept from light and in a cool place. It is intensely poisonous even by inhalation.

Diluted Hydrocyanic Acid is an antispasmodic and sedative, especially in spasmodic cough; also it is used externally in certain skin diseases. Average dose, 0.1 cc.

Mandelic Acid or Racemic Mandelic Acid (U. S. P. 1938 to 1947; N. F. 1947 to date), when dried over sulfuric acid for eighteen hours, contains not less than 99 per cent of $HC_8H_7O_3$.

Mandelic Acid is made from benzaldehyde by interaction with sodium bisulfite and sodium cyanide and subsequent hydrolysis. It occurs as white crystals or powder, has but a slight aromatic odor, and gradually darkens and decomposes on exposure to light. It is freely soluble in water, alcohol, ether and isopropyl alcohol.

Mandelic Acid is used as a urinary antiseptic but is not effective unless the urine is at pH 5.5 or less, hence it is usually given as the ammonium, calcium or sodium salt with ammonium chloride. Dose, 4 gm.

CHERRY

Wild Cherry or Wild Black Cherry Bark (U. S. P. 1820 to date) is the stem bark of *Prunus serotina* Ehrhart, collected in autumn and carefully dried. *Prunus* is the classical name of the plum tree; *serotina* means late or backward, referring to the time of flowering and fruiting of the species.

The plant is a tree growing to the height of 100 feet or more in the eastern United States and Canada, the commercial supplies of the drug coming chiefly from Michigan, Indiana, Virginia and North Carolina.

Borke, the sloughing dead tissue which is caused by the formation of adventitious phellogens occurring in the cortex or even in the phloem region, should be removed, a process known as "rossing." There are two commercial grades of bark on the market, a thick and a thin variety, the latter being preferred. The bark is collected in autumn, and should be carefully dried and preserved in air-tight containers.

Wild cherry bark was used by the Indians and no doubt the early settlers learned its use from them. It has long enjoyed popular usage in domestic medicine.

Description, Structure and Powder.—See Figure 168 and the U. S. Pharmacopœia.

Constituents.—A cyanogenetic glucoside, *l*-mandelonitrile glucoside, a compound formed by the partial hydrolysis of amygdalin (see page 315), and isomeric with sambunigrin (*d*-mandelonitrile glucoside), from the leaves of *Sambucus nigra*, and prulaurasin (*dl*-mandelonitrile glucoside), from the leaves of *Prunus laurocerasus.*

Wild Cherry also contains a ferment resembling emulsin; *b*-methylæsculetin (methyl ether of dihydroxy-coumarin) which probably occurs in combination as a crystalline glucoside, the solutions giving a blue fluorescence; a phytosterol; *l*-mandelic acid; oleic acid; *p*-coumaric acid; tri-methyl-gallic acid; ipuranol; dextrose; sugar; tannin; starch and calcium oxalate. Total ash, about 4 per cent; acid-insoluble ash, about 0.15 per cent. The yield of hydrocyanic acid varies from 0.23 to 0.32 per cent (inner bark) to 0.03 per cent (trunk bark) and varies even in the bark of the same thickness from the same tree. When the exposure is such that the chloroplastids are abundant in the cells of the bark, the percentage of the *l*-mandelonitrile glucoside is higher, whereas when the exposure is such that the cells do not take an active part in photosynthesis the percentage of the glucoside is lower. In the latter case the bark is yellowish brown. On keeping the bark for a year it deteriorates from 10 to 50 per cent.

Uses and Dose.—Wild Cherry is used as a sedative and pectoral. It is also a tonic and an astringent. Average dose, 2 gm.

Adulterants.—Barks of other species of *Prunus* have been admixed with or substituted for Wild Cherry. They are more astringent and less aromatic.

Wild Cherry Fruit consists of small, black drupes, which when ripe are sweet, slightly acid and astringent. They are used in Europe for preparing **Wild Cherry Wine,** which is pleasantly aromatic.

Cherry Laurel, the fresh leaves of *Prunus laurocerasus,* when macerated in water and distilled, forms **Cherry Laurel Water** containing about 0.1 per cent of HCN, and extensively used, especially in Europe, as an anodyne, sedative and antispasmodic, as well as a flavoring agent. Average dose, 1 cc.

Cherry laurel leaves contain about 1.3 per cent of the glycoside laurocerasin; amygdalic acid; emulsin, causing the decomposition of the glycoside, more slowly than amygdalin, and yielding about half as much hydrocyanic acid (about 1.2 per cent) and benzaldehyde (about 0.5 per cent).

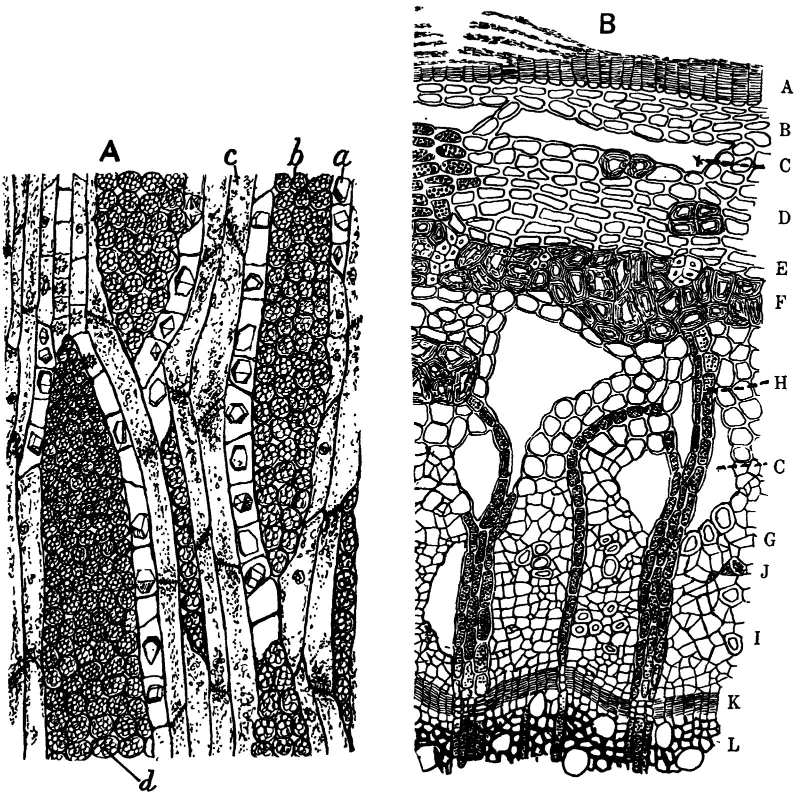


FIG. 168.—*Prunus serotina:* *A*, longitudinal section of inner bark, showing crystals of calcium oxalate (*a*), medullary ray cells containing starch (*b* and *d*), and leptome or sieve (*c*). (After Bastin.) *B*, bark from three-year-old stem: *A*, cork with lenticel; *B*, collenchyma, bearing starch; *C*, intercellular space; *D*, stone cells in small bundles; *E*, primary bast fibers in small bundles; *F*, mixed ring of bast and stone cells; *G*, parenchyma of the phloem; *H*, parenchyma of the medullary ray, bearing starch; *I*, young stone cells; *J*, companion cells and sieve tubes; *K*, cambium; *L*, young xylem. (Drawing by E. N. Gathercoal.)

Cherry or Sour Cherry (N. F. 1936 to 1942) is the fresh, ripe fruit of cultivated varieties of *Prunus Cerasus* Linné. The specific name is from Cerasus in Pontus from which, according to Pliny, Lucullus is said to have introduced *P. cerasus* to grace his triumph over Mithridates. There are many cultivated varieties of this tree, the fruits of which are eaten fresh, canned or used as ingredients in preserves, etc. The trees are cultivated almost universally in the temperate zone. An important commercial source is the fruit belt of Michigan.

The sour cherry fruit is a spherical, depressed, globose or cordate drupe, with a scar at the summit representing the remains of the style, and one at the base representing the point of attachment of the pedicel; up to 20 mm. in diameter; externally pale red to dark red, glabrous; odor of the crushed fruit characteristically aromatic; taste pleasantly acidulous.

The pulp of the cherry contains up to 2 per cent of malic acid; up to 1 per cent of sucrose; about 9 per cent of invert sugar; 0.2 to 0.4 per cent of pectin; and small amounts of citric and tartaric acids. The kernel contains about 28 per cent of protein; 38 per cent of fixed oil; 0.8 per cent of amygdalin and emulsin. Sour cherries have been used in the preparation of syrup of cherry.

Cherry Juice (N. F. 1942 to date) is the liquid expressed from the fresh, ripe fruit of *Prunus Cerasus* Linné.

The cherries are washed, stemmed, but not pitted, and are coarsely ground to break the pits but not mash the kernels; the mixture is preserved with 0.1 per cent benzoic acid and allowed to stand at room temperature (possibly for several days) until the addition to a small portion of the juice of one-half its volume of alcohol produces a clear solution, which does not become cloudy within thirty minutes. This test indicates that the pectin in the juice has been destroyed by enzymic action and that the juice or the syrup made from the juice can be used in medicinal preparations without causing cloudiness due to the presence of alcohol. The pectin-free juice is pressed out from the mixture and filtered to a clear liquid.

Cherry juice contains not less than 1 per cent of malic acid and not less than 10 per cent of dry solids. It is practically free from arsenic and lead.

Cherry juice is used in the preparation of **Cherry Syrup** (N. F. 1936 to date), which serves as a pleasant disguising agent in pharmaceutical mixtures, especially those of an acidulous nature.

BERRIES

Raspberry or Red Raspberries (U. S. P. 1882 to 1905; N. F. 1916 to 1942) is the fresh ripe fruit of varieties of *Rubus idæus* Linné, or of *Rubus strigosus* Michaux. The generic name *Rubus* is Latin for *bramble; idæus* refers to Mt. Ida, and *strigosus* means lean. The plants are prickly perennials commonly cultivated in temperate portions of the United States and Europe. The fruit is collected when ripe in early summer and used while fresh for making the raspberry juice, its only pharmaceutical preparation.

Red Raspberry is a red aggregate fruit, hemispherical or somewhat cone-shaped, hollow or with a concave depression at the base where separated from the receptacle, and composed of 20 or more small, rounded-polygonal succulent drupelets; pericarp with numerous, non-glandular hairs up to 640 microns in length; mesocarp fleshy, with red juice and occasional rosettes of calcium oxalate, the latter up to 35 microns in diameter and occurring in the parenchyma; endocarp hard and wrinkled and enclosing the small seed; odor characteristic, fragrant; taste pleasant, sweet, acidulous.

Red raspberry fruit contains about 2 per cent of malic and citric acids, 4 per cent of levulose, 0.5 per cent of sucrose, 0.4 per cent of pectin substances and a small amount of volatile oil to which its distinct flavor is due.

Raspberry Juice or Red Raspberry Juice (N. F. 1942 to date) is the liquid expressed from the fresh ripe fruit of varieties of *Rubus idæus* Linné or of *Rubus strigosus* Michaux.

The fruit is washed, drained and expressed; the juice is preserved with 0.1 per cent of benzoic acid and allowed to stand at room temperature until the pectin has been destroyed by enzymic action and then filtered to a clear liquid. The juice when mixed with one-half its volume of alcohol produces a clear solution which does not become cloudy within thirty minutes.

Red Raspberry juice contains not less than 1.5 per cent of citric acid and not less than 5 per cent of dry solids. It is practically free from coal tar dyes and from arsenic. The color of the juice fades when exposed to light.

Red Raspberry juice is used in the preparation of **Raspberry Syrup** (U. S. P. 1882 to 1905; N. F. 1916 to date) which serves as a pleasant disguising agent in pharmaceutical mixtures, especially those of an acidulous nature.

Black Raspberries, the fresh, ripe fruit of varieties of *Rubus occidentalis* Linné were permitted, in the N. F. 1916 to 1926, as a substitute, in whole or in part, for Red Raspberries.

Blackberries (N. F. 1916 to 1926), the fresh ripe fruit of varieties of *Rubus nigrobaccus* Bailey or *Rubus villosus* Aiton, were used for the preparation of **Syrup of Blackberry Fruit** (N. F. 1916 to 1926), which was used for the same purposes as the Raspberry Syrups.

Blackberries contain, in addition to the acidulous constituents, some tannin, and the **Blackberry Wine** made from this fruit is valued for its astringency.

Strawberries, the fruit of cultivated varieties of *Fragaria chilœnsis, F. vesca* and *F. virginiana,* contain about the same constituents as red raspberries, and have been used for the preparation of a pleasant acidulous syrup for pharmaceutical use. This syrup is not as acidulous as red raspberry syrup, has never been official, and is used but little.

Rubus or Blackberry Bark (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the dried bark of the rhizome and roots from plants of the section *Eubatus* of the genus *Rubus.* The bark should be collected in spring or autumn and dried. It occurs in elongated, flexible, transversely curved or slightly quilled pieces 1 to 2 mm. in thickness; outer surface deep red-brown or dark gray-brown, longitudinally wrinkled, with few root-scars, periderm frequently exfoliated; inner surface light brown, coarsely longitudinally striate; fracture tough, fibrous, readily splitting; odor slight; taste astringent. It contains tannin, 10 to 20 per cent; gallic acid, about 0.4 per cent; a bitter, crystalline glucoside, villosin, somewhat resembling saponin, about 0.8 per cent; starch; calcium oxalate; total ash, about 3 per cent; acid-insoluble ash, about 0.25 per cent. Rubus is an astringent and a tonic.

Prune (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the fruit of *Prunus domestica,* a small tree indigenous to southern Europe, and largely cultivated in southern France, Germany, Asia Minor and California, but not found growing wild. The ripe fruit is partially dried by artificial means or in the sun. The chief source of our supply is California. It is a superior drupe, fleshy, ellipsoidal, more or less compressed, 3.5 to 4 cm. in length; externally brownish black, glabrous, wrinkled. The sarcocarp is yellowish brown, fleshy, somewhat stringy, and with a sweet and acidulous taste. The endocarp is ellipsoidal, flattened, about 2 mm. in thickness; externally dark brown, reticulate; internally light brown, smooth, 1-locular, 1-seeded, occasionally 2-seeded. The seed is about 2 cm. in length.

Prune contains from 25 to 44 per cent of sugar; organic acids, as malic and tartaric, partly free, about 2 per cent; and about 30 per cent of water. It is a laxative and a nutrient, being usually used medicinally in combination with other remedies.

Prune Pulp was recognized separately in the U. S. P. from 1842 to 1862.

Fresh Apple Juice (N. F. 1916 to 1936) is the freshly expressed juice of sound, ripe, sour apples, the fruit of cultivated varieties of *Pyrus malus.* Apple juice contains malic acid, sugar and varying amounts of pectin. It is a laxative and, especially when employed cold, has refrigerant properties.

Cydonium or Quince Seed (U. S. P. 1851 to 1894) is the ripe seed of *Cydonia vulgaris,* a shrub indigenous to southwestern Asia and extensively cultivated. The generic name refers to Cydonia, an ancient city on the island of Crete.

The seed are removed from the ripe fruits, the latter to be used for preserves and dried. The commercial supplies come chiefly from southern Russia and Portugal. The seeds occur *singly or in agglutinated masses, the individual seeds* being somewhat ovoid and compressed, from 5 to 10 mm. in length and from 2 to 6 mm. in breadth; the outer surface is reddish brown or brownish violet, more or less covered with adhering grayish gum; the fracture is short; the inner surface shows a large yellowish white embryo and a thin, reddish brown seed coat, which is easily separated by placing the seeds in water. It is inodorous and the taste is mucilaginous, slightly aromatic and similar to that of benzaldehyde.

The seed contains mucilage 22 per cent, yielding on hydrolysis, with dilute sulfuric acid, oxalic acid and arabinose. It is distinguished from cherry gum and the mucilages of other *Mimoseæ* by being precipitated upon the addition of creosote water. Upon macerating 1 gm. of cydonium with 50 parts of water, a thick, transparent jelly should form.

Apple and pear seeds are sometimes substituted. They are readily identified by being ovoid, flattened, acute and pointed at the base, of a uniformly dark brown color and not whitish; and having a smooth, shiny outer surface which is not mucilaginous.

Cydonium is used as a demulcent vehicle for other remedies, especially in skin lotions. It is a frequent constituent of so-called "wave sets."

ROSE

Rose, Red Rose, French Rose, or Rosa Gallica (U. S. P. 1831 to 1936; N. F. 1936 to date) is the dried petals of *Rosa gallica* Linné, collected just before the expansion of the flowers. The generic name *Rosa* is the ancient Latin name for the rose; *gallica* means "of or pertaining to Gaul," now France. The plant is a shrub indigenous to southern Europe and probably western Asia, and extensively cultivated in all parts of the world. The petals are obtained from cultivated plants before the expansion of the flower, the lower clawed portion usually being removed; they are used fresh or are carefully dried and preserved. The chief supply of the drug is obtained from southern France. *Rosa gallica* is said to have been introduced into France in 1241 by the Count of Champagne on his return from the Crusades.

DESCRIPTION.—Separate or imbricated, in small cones; petals broadly ovate, the upper part rose-colored and deeply notched, the lower part brownish red, more or less rounded, acute or truncate, with numerous papillæ and fine longitudinal veins; texture velvety; odor agreeable, fragrant; taste astringent and slightly bitter.

STRUCTURE.—See Figure 169.

CONSTITUENTS.—Volatile oil in small amount; a yellow crystalline rhamnoside, quercitrin, which yields, on decomposition, quercetin and rhamnose; tannin and gallic acids. The coloring principle is soluble in water and alcohol and gives a deep yellow-red color with acids, a green color changing to brown with alkalis, purple or violet with potassium alum or iodine solutions, and a deep blue with ferrous or ferric salts. Total ash about 4 per cent; acid-insoluble ash about 0.4 per cent.

STANDARDS.—Rose contains not more than 1 per cent of foreign organic matter, and yields not more than 1 per cent of acid-insoluble ash.

USES AND DOSE.—Rose is a mild astringent and tonic. Average dose, 2 gm.

Rose Oil or Attar of Rose (U. S. P. 1842 to 1916, 1936 to date) is the volatile oil distilled with steam from the fresh flowers of *Rosa gallica*

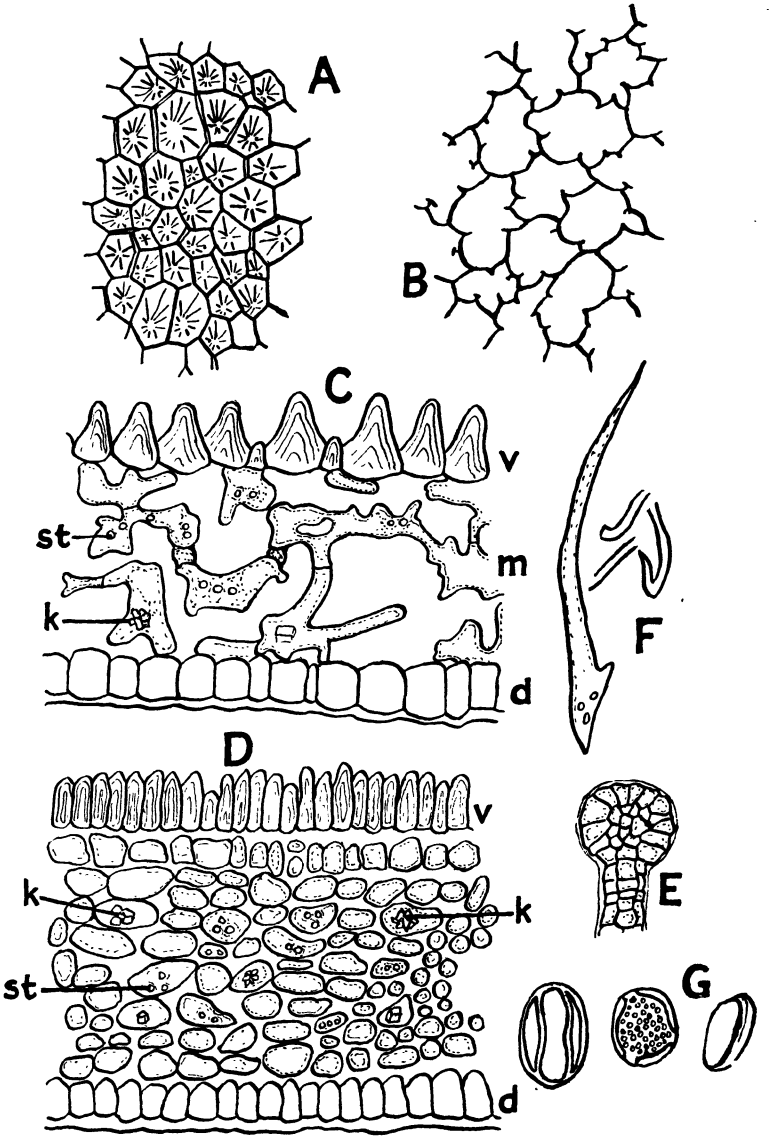


FIG. 169.—*Rosa gallica:* *A*, surface view of the ventral or upper surface of petal, showing polygonal cells, the radiating lines indicating the folds formed by the papillæ. *B*, surface view of cells on the dorsal or lower surface of the petal with inner projections being sometimes of a T-shape. *C*, cross-section from the middle of the petal, showing the upper epidermal cells with papillæ (*v*), loose mesophyll cells (*m*), some of which contain small crystals of calcium oxalate (*k*) and starch grains (*st*), and cells of lower epidermis in which the papillæ are wanting. *D*, transverse section through the base of a petal, the letters as in *C*. Fragments found in the powder show in addition to the cellular elements of the petals, a glandular hair (*E*) and non-glandular hairs (*F*) which occur on the stems and sepals; and pollen grains (*G*). (Re-drawn by Haase from plates of Hans Kramer.)

Linné, *Rosa damascena* Miller, *Rosa alba* Linné and *Rosa centifolia* Linné, and varieties of these species.

Most of the oil of rose is produced in Bulgaria although a small quantity is distilled in southern France and in Turkey. The flowers are gathered in May and June and subjected to steam distillation in tinned copper stills. The oil which rises to the top of the distillate is pipetted off and the water either marketed as rose water or used to distil a subsequent batch of petals. About 3000 kilos of petals are required to produce 1 kilo of oil. The oil is usually marketed in felt-covered containers.

Description.—A colorless or yellow liquid having the characteristic odor and taste of rose. At 25° C. it is a viscous liquid and upon gradually cooling changes to a translucent crystalline mass, which may be easily liquefied by warming. It has a specific gravity from 0.848 to 0.863 at 30° C.; its optical rotation is −1 to −4 degrees in a 100 mm. tube at 25° C.; refractive index, 1.457 to 1.463 at 30° C.

Constituents.—A colorless stearoptene, 15 to 20 per cent, which is solid at ordinary temperatures; the sesquiterpene alcohols geraniol and citronellol, with smaller quantities of esters of these, and other odorous principles.

Uses.—Oil of Rose is a flavoring agent in pharmaceuticals. It is of great importance in the perfume industry.

Stronger Rose Water (Rose Water, U. S. P. 1820 to 1894) (U. S. P. 1820 to date) is a saturated solution of the odoriferous principles of the flowers of *Rosa centifolia* Linné, prepared by distilling the fresh flowers with water and separating the excess volatile oil from the clear, aqueous portion of the distillate. Its odor is best preserved by allowing a limited access of fresh air to the container. The Water is obtained as a by-product, the rose oil being the principal product.

Rosa Centifolia, Pale Rose or Hundred-leaved Rose (Rosa U. S. P. 1820 to 1831) (U. S. P. 1820 to 1905) consists of the petals of *Rosa centifolia* Linné collected after the expansion of the flowers and carefully dried.

Rosæ Caninæ Fructus or Rose Hips are the fresh fruits of *Rosa canina,* a shrub common throughout Europe and the British Isles. The specific name *canina* refers to the fancied shape of the fruit of this species, meaning, "like a dog." It is sometimes called the "dog hip." They are ovoid, from 15 to 20 mm. in length; externally of a red or scarlet color, smooth and shiny, and having at the summit the 5 calyx-teeth, beyond which project the hairy appendages of the achenes; the pericarp is of a fleshy texture, becoming on maturity, especially after frost, soft and pulpy, the pulp of the sarcocarp being of an orange color and an agreeable, acidulous taste; the hollow receptacle bears on its inner surface numerous, small, hard achenes, which, as well as the walls of the former, are covered with unicellular, thick-walled hairs. Rose hips contain citric acid, 3 per cent; malic acid, 8 per cent; mucilage, 25 per cent; an uncrystallizable sugar, 30 per cent; also citrates, malates and mineral salts. They are mildly astringent, refrigerant and diuretic.

QUILLAJA

Quillaja, Soap Tree Bark or Soap Bark (U. S. P. 1882 to 1916; N. F. 1916 to date) is the dried inner bark of *Quillaja Saponaria* Molina. The name *Quillaja* is derived from the Chilean vernacular, *quillai,* meaning "soap," because the bark of the plant forms a lather with water; *saponaria* refers to the same character. The plant is a large tree indigenous to Chile and Peru.

DESCRIPTION, STRUCTURE AND POWDER.—See Figure 170 and the National Formulary.

CONSTITUENTS.—The drug contains two amorphous glucosides amounting to about 9 per cent, which are closely related to saponin—one soluble in alcohol and known as quillajic acid, and the other nearly insoluble in alcohol and known as quillajasapotoxin; both yield the corresponding sapogenins upon hydrolysis. Total ash from 5 to 10 per cent, nearly all of which is soluble in diluted hydrochloric acid.

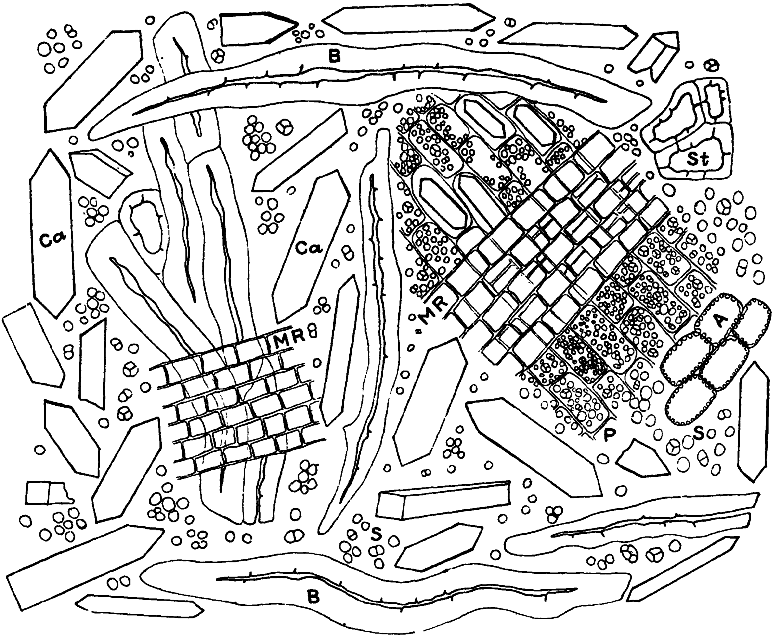


FIG. 170.—Powdered Quillaja: pinkish white; very sternutatory; calcium oxalate in prisms (*ca*) from 35 to 200 microns in length; bast fibers (*B*) numerous, thick-walled, strongly lignified, occasionally with branching ends; crystal fibers containing elongated prisms of calcium oxalate; stone cells (*St*) more or less thick-walled and with simple, oblique pores; starch grains (*S*) nearly spheroidal, from 3 to 10 microns in diameter; parenchyma (*P*) containing starch and calcium oxalate; medullary rays (*MR*) and parenchyma (*A*) with cell walls bearing simple pores.

STANDARDS.—Soap bark contains not more than 5 per cent of adhering outer bark and not more than 1 per cent of foreign organic matter, and yields not more than 2 per cent of acid-insoluble ash.

USES.—Quillaja is used as an emulsifying agent, particularly for tars. It is irritant and expectorant but because of its depressant action on the heart and respiration should not be employed internally.

Brayera, Cusso or Kousso (U. S. P. 1863 to 1916; N. F. 1916 to 1936) is the pistillate flowers of *Hagenia abyssinica*, a tree indigenous to northeastern Africa and cultivated in Abyssinia. The entire panicles are collected soon after pollination and dried in the sun; the flowers are sometimes stripped from the panicles, or the panicles are made into rolls.

The flowers are shown in Figure 171.

The active principle appears to be an amorphous substance, cosotoxin, related to filicic acid; other principles are α-cosin, β-cosin, protocosin and cosidin, the two last being colorless crystalline compounds which are inactive.

Cusso is used as an anthelmintic and as a tænifuge.

Tormentilla (U .S. P. 1820 to 1882) is the rhizome of *Potentilla tormentilla*, indigenous to central and northern Europe and northern Asia. It contains tannic acid from 18 to 30 per cent; tormentilla red, a product of decomposition of the tannin; ellagic acid; a trace of volatile oil and a resin. Tormentilla is used as an astringent and as a tonic.

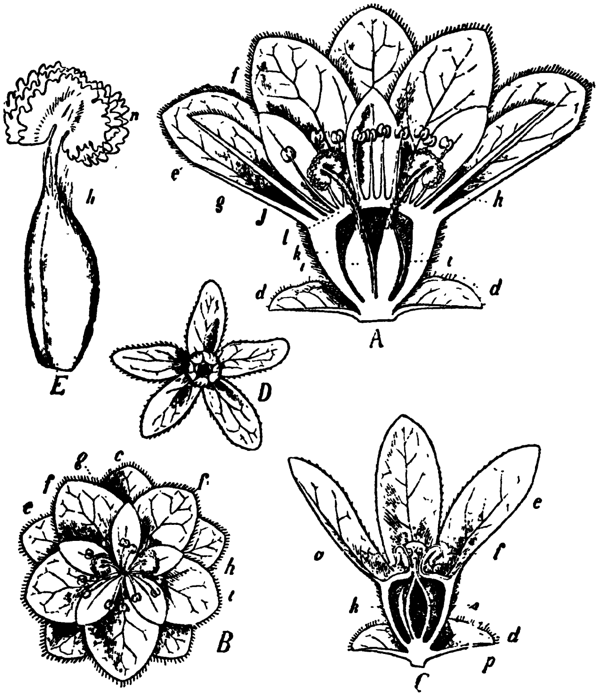


Fig. 171.—Cusso: *A*, longitudinal section through an expanded pistillate flower showing bracts (*d*), outer series of sepals (*e*), inner series of sepals (*f*), petals (*g*), perianth tube (*k*), sterile stamens (*h*), and pistil (*i*). *B*, mature flower viewed from above and showing the relation of sepals and petals. *C*, flower, just before the maturing of the fruit showing pericarp (*p*), and seed (*s*). *D*, mature pistillate flower as seen from above. *E*, pistil showing cylindrical ovary, slender style with hairs (*h*) and large, slightly lobed stigma. (After Meyer.)

Geum or Water Avens (U. S. P. 1820 to 1882) is the dried root of *Geum rivale* Linné, a plant growing in the northern United States.

The perennial root is horizontal, jointed and scaly, about 15 cm. long, with numerous, descending, yellow rootlets. It is reddish brown externally and white internally. It is hard and brittle; inodorous; bitter and astringent. It has been used as an astringent. Dose, 1 to 4 gm.

Spirea or Hardhack (U. S. P. 1820 to 1882) is the root of *Spirea tomentosa* Linné. The plant is a shrub indigenous to eastern United States and Canada and westward to Minnesota and Kansas. The roots are woody, with brown bark and an astringent taste. It has been used as an astringent in doses of 0.5 to 1.5 gm.

LEGUMINOSÆ, OR PULSE FAMILY

This is the second largest family of flowering plants and comprises over 500 genera and about 12,000 species. These are widely distributed, being most numerous in the tropical and subtropical regions. They exhibit a great range of habit, from creeping annual herbs to climbing shrubs, and vary from delicate herbs to very tall trees. The plants are characterized by alternate, stipulate, usually compound leaves; papilionaceous or sometimes regular flowers, having monadelphous or diadelphous stamens and a single free pistil. The fruit is a legume from which the family receives its name.

It is divided into subfamilies as follows:

1. *Papilionaceæ,* with irregular, papilionaceous flowers, and calcium oxalate in the form of styloides or small rod-like crystals, these being not infrequently inserted in the thickened cell walls. Tannin sacs, resin canals, lysigenous gum canals and other secretory cavities occur in the species of this group. About two-thirds of the *Leguminosæ* belong to this subfamily, which yields important drugs and economic products.
2. *Cæsalpinaceæ,* in which the corollas are imperfectly or not at all papilionaceous. These plants usually contain, in addition to solitary crystals, rosette aggregates of calcium oxalate.
3. *Mimosaceæ,* in which the flowers are small and regular; calcium oxalate may occur in the form of rhombohedral crystals or styloides, occasionally being imbedded in the thickened cell wall. Secretion sacs in the phloem strands are common. In some species the walls of the cells of the pericycle, the phloem and wood undergo a metamorphosis into mucilage, which then exudes and collects in the form of tears upon the outside of the bark of the branches. With acacia gum it appears that the cell contents of the pith and medullary ray cells is converted into the mucilage. **Cassie Oil,** used in perfumery, is from this subfamily.

GLYCYRRHIZA

Glycyrrhiza or Licorice Root (U. S. P. 1820 to date) is the dried rhizome and roots of *Glycyrrhiza glabra* Linné var. *typica* Regel et Herder, known in commerce as Spanish Licorice, or of *Glycyrrhiza glabra* Linné var. *glandulifera* Waldstein et Kitaibel, known in commerce as Russian Licorice (U. S. P. 1890 to date), or of other varieties of *Glycyrrhiza glabra* Linné yielding a yellow and sweet wood. *Glycyrrhiza* is of Greek origin and means sweet root; *glabra* means smooth, and refers to the fruit of this species which is a smooth pod. In the species *glandulifera* the fruit has gland-like swellings.

The plant is a perennial herb attaining a height of 1 to 1.7 meters. The underground portion of the variety *typica* (Spanish licorice) consists of several horizontal, spreading rhizomes bearing buds and of branching roots which penetrate the soil to a depth of several feet. In the variety *glandulifera* (Russian licorice) the underground portion consists of a large rhizome which gives off long, thick, fusiform roots.

Until 1870 Spain produced practically the entire world's supply of licorice root. Now most of the countries bordering the north side of the Mediterranean Sea, along with Arabia, Syria and Iran, cultivate the variety *typica;* wild plants of the variety *glandulifera* found on the borders of the Black and Caspian Seas furnish most of the Russian licorice. Experimental lots of licorice root have been produced by cultivation in California and Oregon, where there are great areas well adapted to it, yet until mechanical means reduces the high labor cost the United States will not become a competitor in the production of licorice. Over 75,000,000 pounds of the drug are imported annually, besides 1,500,000 pounds of the licorice extract.

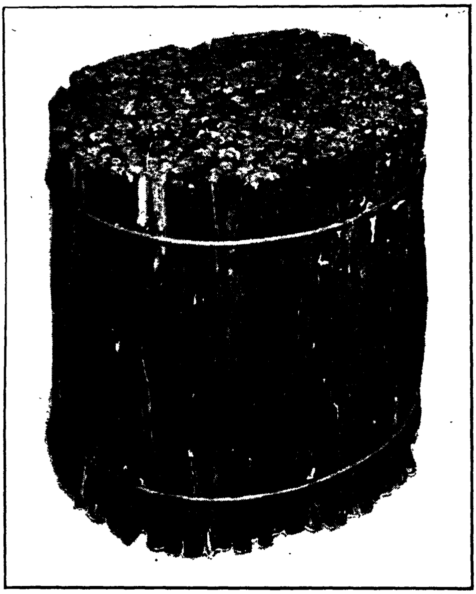


FIG. 172—A bundle of Spanish Licorice root from the Pharmacognosy Museum of the University of Illinois. (Photo by R. S. Adamson.)

Propagation of the variety *typica* is generally by cuttings of the rhizome which are planted in rows about 4 feet apart. At the end of the third or fourth year the rhizome and roots are dug, preferably in the autumn and from plants which have not borne fruit, so as to insure maximum sweetness of the sap. The washed material is air-dried (four to six months), packed into bales or cut and tied into short cylindrical bundles (see Fig. 172). The large thick roots of Russian licorice are peeled before drying. In southern Italy a considerable amount of the crop is extracted with water, the liquid being clarified and evaporated, and the resulting extract molded into sticks, etc.

DESCRIPTION, HISTOLOGY AND POWDER.—See Figures 172, 173, 174 and the U. S. Pharmacopœia.

CONSTITUENTS.—From 3 to 12 per cent of glycyrrhizin; glucose, about 3 per cent; sucrose, about 5 per cent; asparagin, about 3 per cent; mannite and a

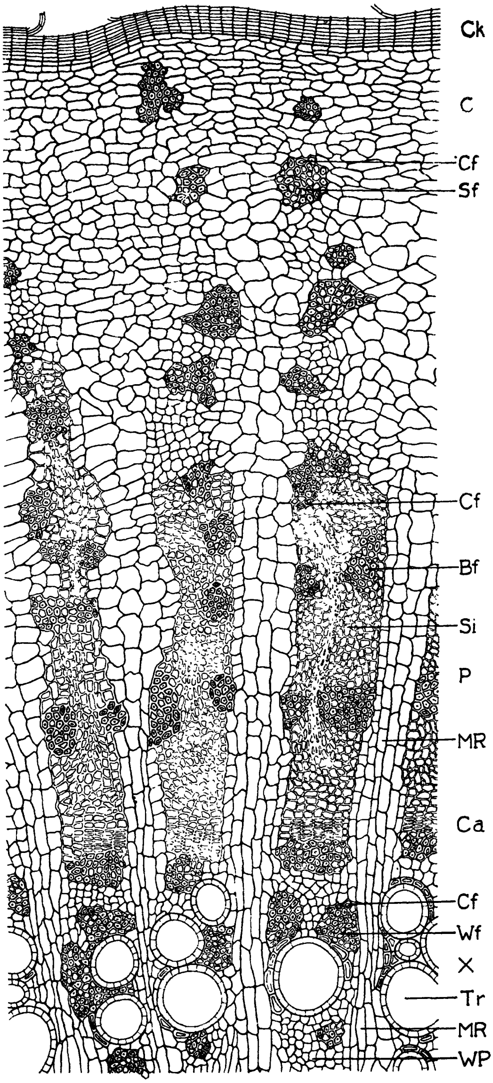


FIG. 173.—Spanish Licorice in transverse section: *Ck*, cork of numerous layers of yellowish brown cells; *C*, cortex, with outer rows collenchymatous and inner portion parenchymatous, with groups of fibers (*Sf*), more or less surrounded by crystal fibers (*Cf*); *P*, phloem with alternating strands of bast (*Bf*) and sieve (*Si*), the cells of the latter with thickened highly refractile walls; *MR*, medullary rays from 1 to 8 cells wide and definitely radiate, alternating with the phloem; *Ca*, cambium, narrow and inconspicuous; *X*, xylem region with broad wood wedges containing bundles of wood fibers (*Wf*) associated with crystal fibers (*Cf*), large tracheæ (*Tr*) and thin-walled, non-lignified wood parenchyma (*WP*); the parenchyma cells of the bark, medullary rays and wood bear an abundance of starch. (Drawing by Harry Flower.)

bitter principle known as glycyramarin, which occurs principally in the bark and hence is less abundant in the Russian licorice.

Standards.—Glycyrrhiza yields not more than 2.5 per cent of acid-insoluble ash.

Uses and Dose.—Glycyrrhiza is a demulcent, an expectorant and a mild laxative. It is considerably used as a flavoring agent and is frequently used to mask the taste of such drugs as aloe, ammonium chloride, quinine, etc.

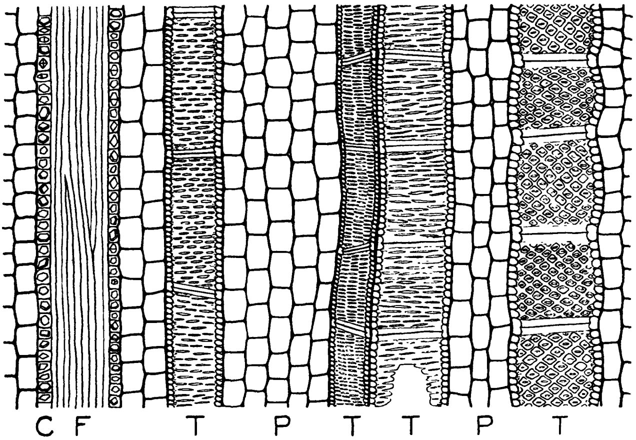


Fig. 174.—Spanish Licorice in longitudinal section through the xylem region: *C*, crystal fibers; *F*, wood fibers; *T*, reticulate and dotted tracheæ; *P*, starch-bearing parenchyma. (Drawing by Harry Flower.)

Glycyrrhiza Extract, Extract of Licorice, or Licorice (U. S. P. 1820 to date) is a commercial extract prepared by extracting coarsely ground licorice root, usually the inferior grades, with warm water, clarifying the extract and evaporating it almost or quite to dryness. Spanish licorice is used almost exclusively for preparing this extract.

Glycyrrhiza extract occurs as a brown powder or in flattened, cylindrical rolls or in masses. The rolls and masses have a glossy black color externally and a brittle, smooth, conchoidal fracture; the taste is sweet and characteristic. Not less than 75 per cent of the extract is soluble in cold water. It contains no foreign starch and yields not more than 5 per cent of ash.

Extract of licorice is used as an excipient in the manufacture of pills and troches and as a flavoring and disguising agent in other pharmaceutical preparations. Much of the commercial supply is used in confectionery and in chewing tobacco.

Ammoniated Glycyrrhizin (U. S. P. 1882 to 1926) is glycyrrhizin combined with ammonia, and occurs as dark brown or brownish red scales, without odor, but having a very sweet taste. It is freely soluble in water and in alcohol. An aqueous solution supersaturated with an acid precipitates glycyrrhizic acid ($C_{44}H_{64}O_{19}$). In the plant this acid is combined with calcium or potassium to form glycyrrhizin. Glycyrrhizic acid occurs as an amorphous, yellow powder, having a strong bitter-sweet taste and an acid reaction. A saturated solution in hot water forms a jell on cooling. Boiled with dilute sulfuric acid it yields glycyrrhetic acid and glycuronic acid, but no sugar, hence it is not a true glycoside. However, glycuronic acid is an oxidation product of glucose.

Wild or American Licorice is the root of *Glycyrrhiza lepidota*, a perennial herb indigenous to western North America. The plant is similar to that yielding Spanish licorice. The roots contain 6 per cent of glycyrrhizin and considerable glycyramarin. It has never been substituted for the official licorice.

Manchurian Licorice is the root of *Glycyrrhiza uralensis* of Siberia; the drug is claimed to be only slightly inferior to the best kind of Russian licorice.

Other Leguminous plants that contain principles similar to glycyrrhizin are **Indian or Jamaican Licorice** from *Abrus precatorius* of India and the West Indies; the root of *Ononis spinosa*, a perennial herb of Europe, and other species of *Ononis* as well; the locust (*Robinia pseudacacia*) of the United States and Canada (see page 360); *Caragana pygmæa* of Siberia and northern China; *Hedysarum americanum* of the northern United States and Canada; *Periandra mediterranea*, and *P. dulcis* of Brazil and Paraguay; and Wild Licorice, *Galium circæzans*; also the root of the English walnut, *Juglans regia* (Fam. *Juglandaceæ*); and the rhizome of *Polypodium vulgare* (Filices).

Gums and Mucilages

A short discussion of gums and mucilages is introduced at this point because the two principal items in this class of drug products are Tragacanth and Acacia which come from this family.

Gums are translucent, amorphous substances usually produced by plants as a protective after injury. They, together with the mucilages, pectins and celluloses belong to a class of substances which are condensation products of the pentoses. They may be pentosans, having the formula $(C_5H_8O_4)_n$ or hexosans, having the formula $(C_6H_{10}O_5)_n$, or combined pentosan-hexosans. The gums, when hydrolyzed, yield large proportions of sugars and also contain a complex organic acid nucleus, by means of which they form salts with calcium, magnesium, etc. Gums are precipitated from solution by alcohol and lead subacetate solution.

An effort has been made to distinguish between mucilages and gums on the basis that gums readily dissolve in water and mucilages do not dissolve, but form slimy masses. Others have tried to distinguish between them on the basis that gums are physiological products and mucilages are pathological products, but this classification has not been very successful. It is interesting to note that pectins, which are closely related to gums and mucilages, form aqueous colloidal solutions which are easily converted into "jellies;" cellulose is unaltered in water.

Mucilages are generally sulfuric acid esters where the ester group is a complex polysaccharide. Both gums and mucilages are generally considered as decomposition products of cellulose.

Gums and mucilages are closely related to the hemicelluloses in composition and function except that where the principal sugars produced by hemicelluloses are glucose, mannose and xylose, those produced by gums and mucilages are galactose and arabinose. Gums and mucilages also contain various uronic acids. Acacia and damson gum contain glucuronic acid units and the mucilages from elm bark and linseed contain galacturonic acid. Pectins are also composed of polygalacturonic acid units and sugars. The mucilages found in seaweeds (agar; chondrus) consist of salts of alginic acid, the latter containing *d*-mannuronic acid residues.

Gums and mucilages are produced in various ways by the plant which may be noted as follows:

1. Formed from the middle lamella as in the algæ:
    - Agar, 65 per cent gelose.
    - Chondrus, 55 to 80 per cent carrageenin.
    - Fucus, 22 to 65 per cent mucilage.
    - Laminaria, about 50 per cent mucilage.
2. Formed from the cell wall:
    - (*a*) Of the seed epidermis:
        - Linseed mucilage.
        - Quince seed mucilage.
        - Psyllium seed mucilage.
    - (*b*) Of the seed endodermis:
        - Fenugreek.
    - (*c*) Of cells in the bark:
        - Slippery elm mucilage.
        - Cinnamon mucilage.
3. Formed in special secretion cells:
    - Squill.
4. Formed in schizogenous sacs:
    - Young stems of *Rhamnus purshiana.*
5. Formed by lysigenous metamorphosis of the cell walls:
    - Tragacanth.
    - Acacia.
    - Sterculia gum.
    - Ghatti gum.
    - Cherry gum.
    - Mesquite gum.

TRAGACANTH

Tragacanth or Gum Tragacanth (U. S. P. 1820 to date) is the dried gummy exudation from *Astragalus gummifer* Labillardiere, or other Asiatic species of *Astralagus.* The name tragacanth is from the Greek *tragos* (goat) and *akantha* (horn) and probably refers to the curved shape of the drug; *astragalus* means milk-bone and refers to the exuding and subsequent hardening of the drug; *gummifer* is Latin, meaning gum-bearing. The plants are thorny branching shrubs about one meter in height, and are abundant in the highlands of Asia Minor, Iran, Kurdistan, Syria, Armenia and Greece. When the plant is injured the cell walls of the pith and then of the medullary rays are gradually transformed into gum. This absorbs water and creates internal pressure within the stem, thus forcing the gum to the surface through the incision causing the injury. When the gum strikes the air it gradually hardens due to the evaporation of the water. The nature of the incision governs the shape of the final product. That exuding from natural injuries is more or less worm-like and twisted into coils (**vermiform tragacanth**) or in irregularly shaped tears (**tragacanth sorts**) of a yellowish or brownish color. The better grade is from transverse incisions in the main stem and older branches made with a knife. The gum from such incisions is ribbon-like, showing longitudinal striations caused by small irregularities in the incision. The metamorphosis takes place only at night and the tragacanth ribbons exhibit transverse striations showing the amount that exudes each night. The shorter the time of drying the whiter a more translucent the ribbons will be. This ribbon form of tragacanth is graded commercially by numbers, No. 1 being almost colorless (white) and nearly translucent; No. 2 and No. 3 have more color and opaqueness. Tragacanth was known to Theophrastus (300 B.C.) and Dioscorides and seems to have been used during the Middle Ages. It was not until very recent times, however, that the natives learned to clean the bases of the bushes and incise the bark with a knife, thus producing the clean, white, semi-transparent product of present day commerce. The principal points of export are Smyrna and various ports along the Persian Gulf. That obtained from the latter is known as **Persian or Syrian Tragacanth** and is preferred.

DESCRIPTION.—In flattened, lamellated, ribbon-like pieces, from 0.5 to 3 mm. in thickness; irregularly oblong, more or less curved; externally nearly colorless to weak yellow, with numerous concentric ridges or lamellæ; translucent; fracture short, tough, horny; rendered more easily pulverizable by a heat of 50° C. Pieces of the gum softened in water and mounted in glycerin show numerous lamellæ and a few starch grains.

POWDER.—White to yellowish white; inodorous; taste insipid and mucilaginous; slowly affected by water; starch grains mostly single, occasionally 2- or 4-compound, the individual grains spheroidal or ellipsoidal, from 3 to 25 microns in diameter, some being swollen and more or less altered.

CONSTITUENTS.—Bassorin, 60 to 70 per cent, which swells in water but does not dissolve and which gives tragacanth mucilage its peculiar density, serving to distinguish it from acacia, which contains little or no bassorin; a gum, a soluble compound of arabic and ironic acids, about 30 per cent; total ash, 1.5 to 3 per cent, mostly soluble in diluted hydrochloric acid.

STANDARDS AND TESTS.—(1) Tragacanth in 50 parts of distilled water swells and forms a smooth, nearly uniform, stiff, opalescent mucilage free from cellular fragments. (2) Powdered tragacanth shows few or no fragments of lignified vegetable tissue. (3) Boil 1 gm. of tragacanth with 20 cc. of distilled water until a mucilage is formed, then add 5 cc. of hydrochloric acid and again boil the mixture for five minutes; it develops no pink or red color. These tests all serve to detect sterculia (karaya) gum which contains lignified vegetable tissue, gives a more or less stringy mucilage and reacts pink with hydrochloric acid. Powdered tragacanth has been adulterated with cereal starches.

USES.—Tragacanth is a demulcent. It is employed pharmaceutically as a suspending agent for insoluble powders in mixtures; as an emulsifying agent for oils and resins; and as an adhesive in pill and troche masses. It is also employed in cosmetics (hand lotions), as an emollient, and in calico printing, confectionery, etc.

Sarcocolla is a gummy exudation of *Astragalus sarcocolla* and *A. mucronata*, small shrubs indigenous to southern and central Africa. The gum occurs in small, globular, yellowish red or brownish red friable grains, which are often agglutinated into masses and admixed with a few hairs. Sarcocolla has a licorice-like taste. It is soluble in water and alcohol, and contains an uncrystallizable principle, sarcocollin, having a taste of glycyrrhizin; a resin and a gum.

KINO

Kino (U. S. P. 1820 to 1942; N. F. 1942 to date) is the dried juice obtained from the trunk of *Pterocarpus Marsupium* Roxburgh. The name *Pterocarpus* is Greek and signifies a winged carpel or fruit; *Marsupium* is Latin, meaning a bag or pouch and refers to the shape of the fruit; *kino* is the native name given the drug by the Mandingo tribe of West Africa.

The plant is a large timber tree growing in central and eastern India and in Ceylon. The genus is widely distributed over the earth, and astringent drugs from these species, as well as from other plants not even remotely related to *Pterocarpus,* have come to be known by the name kino.

The phloem contains secretory cells with a red astringent fluid which exudes from the surface when the bark is injured. Vertical incisions are cut into the bark which terminate at their lower end into an oblique incision from which the juice is collected in cups. This juice is dried in shallow pans in the sun and the drug is shipped from Bombay. That shipped from Madras is known as Malabar or East Indian Kino. The drug has been used as an astringent in India from time immemorial. Kino from an African species (*Pterocarpus erinaceous*) was introduced into commerce in 1757.

DESCRIPTION.—Small, angular, opaque or translucent, glistening, brittle pieces, less than 10 mm. in diameter, nearly free from dust, and reddish black to dusky brown in color; thin laminæ appear transparent and ruby-red on the edges; inodorous; sweetish, very astringent and adhering to the teeth when chewed, the saliva being colored red. Kino partially dissolves in water, the solution becoming deep red in color, and leaving numerous small granules, small rod-shaped bacteria and a few indistinguishable plant tissues. In alcoholic mount the red color of the fragments deepens, the translucency increases, and the sharp angular outlines are preserved while solution takes place.

CONSTITUENTS.—Kinotannic acid (see page 215), 30 to 80 per cent; kinoin, 1.5 per cent; catechol (pyrocatechin); kino red; gallic acid; resin; gum; pectin; 13 to 15 per cent of moisture; and an oxydase enzyme which may cause gelatinization of galenicals made from kino, by converting the kinotannic acid into kino red, an insoluble, amorphous red phlobaphene. Kino gives a blackish-green color and precipitate with ferric chloride solution, and a violet color with solutions of ferrous salt.

STANDARDS.—Kino yields not less than 60 per cent of alcohol-soluble extractive and not less than 75 per cent of water-soluble extractive.

USES AND DOSE.—Kino is an astringent. Average dose, 0.5 gm.

African or Gambia Kino is obtained from *Pterocarpus erinaceous* of Senegambia.

Butea or Bengal Kino is obtained from *Butea frondosa,* a tree of western India and Indo-China.

Jamaica Kino is obtained from *Coccoloba uvifera* (Fam. *Polygonaceæ*).

Australian Kino (Red Gum or Eucalyptus Gum) is obtained from species of *Eucalyptus* (see page 450).

RED SAUNDERS

Red Saunders (U. S. P. 1820 to date) is the heartwood of *Pterocarpus santalinus* Linné filius. The specific name *santalinus* is probably from the Persian *sandul,* meaning useful; *rubrum* is Latin, meaning red. This is a large tree growing in southern India, Ceylon and the Philippines. The heartwood is highly prized for cabinet work, and the Indian Government carefully regulates cutting, new forests being established from time to time to prevent extermination. The light-colored sapwood is separated and only the heartwood is employed. Most of the commercial supplies come from Madras.

Red Saunders is mentioned under the name of *Chandana* in the Nirukta, the oldest vedic commentary extant, written not later than the fifth century B.C. Marco Polo refers to sandalwood imported into China, distinguishing the variety by the word *red*. Garcia de Orta of Goa (sixteenth century) distinguishes between the fragrant sandalwood of Timor (see Santalum Album) and the inodorous red sandalwood. In the Middle Ages red saunders was used for coloring purposes, a use to which it is put today.

DESCRIPTION.—Usually in a coarse powder of a reddish orange or brownish red color; in transverse section the wood [illegible], with numerous alternate lighter and darker concentric rings; medullary rays one cell wide; fracture hard, fibrous.

POWDER.—Inodorous; taste slight; wood fibers numerous, mostly irregular in outline with sharply pointed and occasionally forked ends, from 300 to 750 microns in length, walls very thick, porous, yellowish, unevenly thickened and strongly lignified, and the lumina filled with a fine, granular content; tracheæ few with simple or bordered pores and filled with light yellow, resinous masses; occasionally fragments showing medullary ray cells in narrow elliptical groups 1 cell wide and from 3 to 6 cells deep; crystal fibers few with calcium oxalate in the form of monoclinic prisms, from 8 to 20 microns in length. Mounts in chloral hydrate T.S. are of deep, rich-red color.

CONSTITUENTS.—Santalin (santalic acid), which occurs in red needles that are insoluble in water, soluble in alcohol, forming a deep red solution which is colored violet with solutions of the alkalis; tannin; and several colorless crystalline principles. Total ash, about 1 per cent; acid-insoluble ash, about 0.25 per cent.

STANDARDS AND TESTS.—Add 0.5 gm. of red saunders to 10 cc. of alcohol: the mixture becomes distinctly red. Add 0.5 gm. of red saunders to 10 cc. of ether: the solution assumes an orange-yellow color, and when held in a bright light shows a distinct greenish fluorescence. Add 0.5 gm. of red saunders to 10 cc. of distilled water, agitate and filter the mixture: the filtrate remains clear and colorless.

USES.—Red Saunders is used for imparting color.

African sandalwood or barwood is obtained from *P. santalinoides* of tropical West Africa. **Cam-wood or African red-wood** (obtained from *Baphia nitida*, in Sierra Leone) is also valued on account of its red coloring principle.

PERUVIAN BALSAM

Peruvian Balsam, Balsam of Peru, or Peru Balsam (U. S. P. 1820 to date) is obtained from *Myroxylon Pereiræ* (Royle) Klotzsch. *Myroxylon* is from the Greek *myron*, meaning ointment and *xylon* meaning wood; *Pereiræ* is in honor of Jonathan Pereira (1804–1853), an English pharmacognocist. "Peru" refers to the early importation of the balsam into Spain via Lima, Peru.

The balsam trees attain the height of about 25 meters and are especially abundant along the coast of San Salvador in Central America. The tree has been naturalized in Florida and in Ceylon. It is frequently referred to by writers covering the conquest of Guatemala in 1524. In the seventeenth century the drug appeared in German pharmacy, after which its use became universal.

The balsam is a pathological product and is formed by injury to the trees. The tree is beaten on four sides, then scorched with a torch to cause the bark to separate from the trunk, four intermediate strips being left uninjured so as not to kill the tree; within a week the bark drops from the trunk and the balsam begins to exude freely from the exposed wood. The areas are then wrapped with rags which are removed from time to time when they become saturated with balsam; then they are boiled with water and as the water cools, the balsam settles out, is recovered, strained and packed, usually in tin cans. Most of the commercial supply comes from Salvador, although some is produced in Honduras.

DESCRIPTION.—A dark brown, viscid liquid, reddish brown and transparent in thin layers; free from stringiness or stickiness; of an empyreumatic, aromatic, vanilla-like odor; and a bitter, acrid, persistent taste. Soluble in alcohol, in chloroform, in glacial acetic acid, and partially soluble in ether and petroleum benzin. Specific gravity 1.15 to 1.17 at 25° C.

CONSTITUENTS.—Cinnamein, about 60 per cent, which is a volatile oil consisting chiefly of benzyl cinnamate, and lesser amounts of benzyl benzoate and cinnamyl cinnamate; resin esters 30 to 38 per cent, mostly peru-resinotannol cinnamate with a small quantity of the benzoate; vanillin, free cinnamic acid, peruviol, etc., in small amounts.

STANDARDS AND TESTS.—Peruvian balsam yields not less than 50 nor more than 60 per cent of cinnamein, of which the saponification value is between 230 and 240. The acid value of Peruvian balsam lies between 56 and 84. It should be free from oil of turpentine, rosin and fixed oils.

USES.—Peru balsam is an anti-parasiticide in certain skin diseases. It is an antiseptic and vulnerary and is applied externally, either alone or in alcoholic solution, also in the form of an ointment. Internally it is a stimulating expectorant. Its internal use is rather rare.

TOLU BALSAM

Tolu Balsam, Tolu, or Balsam of Tolu (U. S. P. 1820 to date) is obtained from *Myroxylon Balsamum* (Linné) Harms.

The balsam trees grow abundantly along the lower Magdalena River, Colombia. According to Tschirch, the plants yielding Tolu and Peru balsams are physiological varieties of the same species. Tolu is a district near Cartagena, where the balsam was once extensively produced.

Balsam of Tolu is usually considered to be a pathological product similar to balsam of Peru or coniferous oleoresins. V-shaped incisions are made through the bark and sap wood and calabash cups are placed to receive the flow of balsam. Similar cuts are made higher up on the trees, sometimes as many as twenty incisions being made on one tree. The balsam is collected from the cups and transferred to tin containers in which it is shipped.

Some balsam of Tolu is also produced in Venezuela and New Granada and the trees are now being cultivated in the West Indies. Tolu balsam was found in use by the natives upon the discovery of what is now Colombia and Venezuela by the Spanish. Monardes (1574) describes its collection, stating that the drug was much esteemed by the Indians and later by the Spanish, who introduced it into Europe.

DESCRIPTION.—A plastic solid, which gradually hardens, becoming yellowish or reddish brown; transparent in thin layers; pulverizable when old, dried or exposed to cold, and showing numerous crystals of cinnamic acid; odor agreeably aromatic, suggesting that of vanilla; taste aromatic, slightly pungent. Soluble in alcohol, acetone, chloroform and solutions of potassium hydrate.

Constituents.—Resin esters, 75 to 80 per cent, chiefly tolu-resinotannol cinnamate with a small quantity of the benzoate; volatile oil, 7 to 8 per cent, chiefly benzyl benzoate; free cinnamic acid, 12 to 15 per cent; free benzoic acid, 2 to 8 per cent; vanillin, and other constituents in small quantities.

Standards.—Tolu balsam has an acid value of not less than 112 and not more than 168, and a saponification value of not less than 154 and not more than 220. It should be free from rosin, rosin oil or copaiba.

Uses.—Tolu is an expectorant; it is extensively used as a pleasant flavoring in medicinal syrups, confectionery, chewing gum and perfumery.

CHRYSAROBIN

Chrysarobin (U. S. P. 1882 to date) is a mixture of neutral principles obtained from Goa powder, a substance deposited in the wood of *Andira Araroba* Aguiar. *Andria* is of Portuguese origin; *Araroba* is the Latinized East Indian name of the bark, *aroba; Chrysarobin* is from the Greek *Khrysos,* meaning gold, and from *aroba.* Goa is the Portuguese colony on the Malabar Coast to which the plant was imported in 1852. This is a large tree found in the provinces of Bahia and Sergipe in Brazil.

Goa Powder arises in the living cells of the wood of the stems. The cell walls become metamorphosed and finally disintegrated, forming large lacunæ, in which are deposited the altered products in the form of a yellowish brown powder, which is more or less admixed with the tissues of the bark and wood. The trees are hewn and cut into convenient pieces, the Goa powder being scraped out. The crude article is purified by sifting it free from fragments of wood, drying and powdering.

Goa powder is of a light yellow color when fresh, but on exposure to air becomes dark brown or brownish purple. It is composed of small, wine-colored, somewhat translucent, irregular, angular fragments, with a few fragments of tracheæ and libriform cells having bordered pores. It is nearly insoluble in water, but soluble in alcohol, chloroform and solutions of the alkalis, the latter being colored deep red and showing a green fluorescence. It contains from 50 to 75 per cent of a neutral principle, chrysarobin; about 2 per cent of resin; 7 per cent of bitter extractive; a small amount of chrysophanic acid, and yields about 3 per cent of ash. Under the microscope the powder sometimes shows colorless prismatic crystals.

Chrysarobin is prepared by extracting Goa powder with hot benzene, evaporating the solution to dryness and powdering. It is a brownish to orange-yellow microcrystalline powder, odorless and tasteless but irritating to the mucous membrane.

Constituents.—Chrysaphanolanthrone or chrysaphanolanthranol, 30 to 40 per cent; emodinanthrone-monomethyl ether, about 20 per cent and dehydroemodinanthrone-monomethyl ether, about 30 per cent; these compounds are related to the anthraquinones, and chrysarobin has a laxative action although it is not suitable for internal use.

Standards and Tests.—Chrysarobin dissolves in solutions of the alkali hydroxides and in sulfuric acid producing deep red solutions. Place about 2 mg. of chrysarobin on a tile and add 2 drops of fuming nitric acid: the mixture is reddish brown; now add a few drops of ammonia T.S. and an intense violet color is produced. This test serves to differentiate chrysarobin (or Goa powder) from chrysophanic acid and other anthraquinone compounds or anthraquinone drugs.

USES.—Chrysarobin is an irritant and an antiparasiticide. It is used externally. Since it stains badly it should not be used on the face.

PHYSOSTIGMA

Physostigma, Calabar Bean, or Ordeal Bean (U. S. P. 1873 to 1926) is the dried ripe seed of *Physostigma venenosum* Balfour, yielding not less than 0.15 per cent of the alkaloids of Physostigma.

The name *Physostigma* is from the Greek meaning an inflated or bladder-like stigma (see Fig. 175); *venenosum* is from the Latin, meaning full of poison. The plant is a perennial, woody climber growing on the banks of streams in Western Africa, particularly in the vicinity of the Gulf of Guinea. In 1846 Daniell described the use of the seed, known as *esere* by the natives of old Calabar, to prove the innocence or guilt of persons accused of crime. The plant was not classified until 1860.

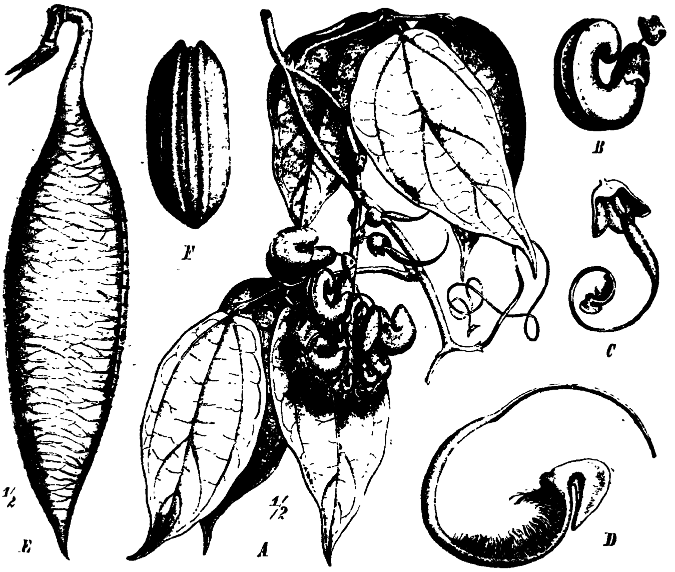


FIG. 175.—*Physostigma venenosum:* *A*, flowering branch; *B*, a single flower; *C*, flower showing ovary and part of the calyx; *D*, enlarged view of style and stigma; *E*, legume; *F*, seed. (After Bentley and Trimen.)

The seed is anatropous, somewhat reniform or irregularly oblong or ellipsoidal, 25 to 30 mm. in length. A brownish black groove from 1 to 2 mm. in diameter extends about half way around the edge, containing the raphe as a narrow line, the micropyle occurring near one end of the groove as a slight depression. The seed coat is brownish red, hard, thick, smooth, but somewhat rough near the groove. Reserve layers are wanting and the embryo is large, white, with a short hypocotyl and two concavo-convex cotyledons. The drug is inodorous and the taste starchy.

The embryo contains numerous starch grains, from 10 to 100 microns in diameter, ellipsoidal or somewhat reniform, and usually with a distinct cleft and frequently with radiating or irregular fissures.

Calabar bean contains starch; proteins; a small amount of fixed oil; several alkaloids, of which physostigmine is the most important; several phytosterol glucosides; a mixture of fatty acids; sugars and resinous material. Total ash about 3.5 per cent; acid-insoluble ash about 0.1 per cent.

Physostigmine Salicylate or Eserine Salicylate (U. S. P. 1882 to date) occurs in colorless or faintly yellow, shining, odorless crystals. It crystallizes from chloroform in rhombohedra (Fig. 176), which are colored red by solutions of the alkalis and yellow by sulfuric or nitric acid. See the U. S. Pharmacopœia for solubilities and tests.

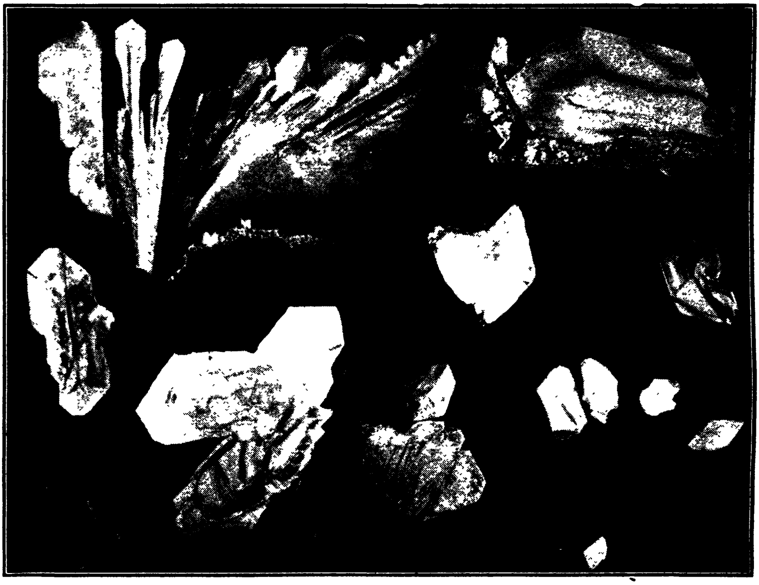


FIG. 176.—Physostigmine salicylate: orthorhombic crystals from a solution in chloroform.

USES AND DOSE.—Physostigmine salicylate is a myotic. It stimulates peristalsis and glandular secretions. Average dose, 2 mg.

Physostigmine Sulfate, or Eserine Sulfate (U. S. P. 1894 to 1916) contains about 20 per cent more of the physostigmine than does the salicylate. It is much preferred by veterinarians and is used subcutaneously as a laxative and for gastric and intestinal catarrh.

ALLIED PLANTS.—The seeds of *P. cylindrospermum* have been substituted for Calabar bean; they are nearly cylindrical and are said also to contain physostigmine.

The lenticular, brown, glossy seeds of *Entada scandens* contain saponin and have been offered as a substitute for physostigma. *Canavalia obtusifolia*, of the East Indies, is also said to have been used as an adulterant of physostigma.

SCOPARIUS

Scoparius, or Broom Tops (U. S. P. 1831 to 1916; N. F. 1916 to 1936) consists of the dried tops of *Cytisus scoparius* (Linné) Link. The plant is a shrub growing in Europe and western Asia and naturalized in the United States. The tops are gathered before flowering and carefully dried. While some of the drug is gathered in Oregon, most of the commercial supplies are imported from Britain or southern Europe.

Scoparius branches are alternate, pentangular, 1 to 3 mm. in thickness; externally dark green, with 5 yellowish green wings and numerous reddish brown cork patches, the younger branches somewhat pubescent; they are usually cut into short pieces.

The leaves are elliptical, obovate, simple, about 5 to 10 mm. in length, digitately trifoliate below; upper surface dark green, nearly glabrous; under surface slightly pubescent; the petiole is wanting in the simple leaves and is about 5 mm. in length in the compound leaves, and pubescent; the drug has a peculiar odor and bitter taste.

Powdered scoparius is dark green with 1-celled non-glandular hairs up to 700 microns long, and thick-walled tracheæ with slightly lignified spiral or double spiral thickenings; narrow, thin-walled sclerenchymatous fibers with simple pores; and fragments of leaf and stem tissue composed of chlorenchyma and epidermis, the latter with broadly elliptical stomata up to 35 microns in length.

The drug contains the volatile, liquid alkaloid sparteine (0.3 per cent); the yellow crystalline flavone scoparin; and about 3 per cent of ash.

Sparteine Sulfate (U. S. P. 1894 to 1926; N. F. 1926 to date), $C_{15}H_{26}N_2.H_2SO_4.5H_2O$, gives sparteine 55.45 per cent, sulfuric acid 23.22 per cent, and water 21.33 per cent; it occurs in colorless rhombohedral crystals or white crystalline powder, is odorless and somewhat bitter in taste. Consult the National Formulary for constants, standards and tests.

Sparteine sulfate is used, particularly by veterinarians, as a cardiac tonic and diuretic. Average dose for humans, 30 mg.; for horses, 1 to 4 gm.

ALLIED PLANTS.—Several plants of the *Leguminosæ* are used like scoparius. Spanish broom is obtained from *Spartium junceum*, a shrub indigenous to the Mediterranean region. *Coronilla scorpioides* yields a yellow glucoside, coronillin.

TONKA

Tonka or Tonquin Beans are the ripe seeds of *Coumarouna odorata* (Dutch Tonka) and *C. oppositifolia* (English Tonka), trees growing in the Amazon region and north to Guiana. The fruits are crushed between stones, the seeds separated and dried in the sun, then steeped in rum or other alcoholic liquors, and by a process of fermentation the fragrant principle, coumarin, is developed; when the seeds are dried coumarin tends to crystallize upon their surface.

Tonka beans are oblong-ovoid, somewhat flattened, 3 to 4 cm. in length and about 1 cm. in width, externally nearly black, usually covered with crystals of coumarin, the coriaceous testa being deeply wrinkled. Internally they are yellowish brown, consisting of two plano-convex cotyledons, enclosing a plumule with two pinnately compound leaves and a fleshy radicle which is directed towards the micropyle situated at the rounded end of the seed. The odor of the seed is fragrant and the taste aromatic and somewhat pungent.

Tonka contains from 1 to 10 per cent of coumarin, about 25 per cent of fixed oil, starch, sitosterin, stigmasterin, sugar and gum; ash from 3 to 4 per cent.

Tonka is used mainly as a flavor; it is an adulterant of vanilla. It is said to be a narcotic stimulant.

Coumarin (N. F. 1916 to date), $C_9H_6O_2$, is the lactone of orthohydroxy cinnamic acid. It occurs in colorless, prismatic crystals, with a characteristic fragrant odor and a bitter, aromatic burning taste. It is soluble in alcohol, ether and chloroform and melts between 67° and 69° C.

Coumarin is obtained from tonka, where it is apparently developed from a mother substance contained in the fixed oil; it is also prepared synthetically from salicyl-aldehyde by boiling it with acetic anhydride and anhydrous sodium acetate.

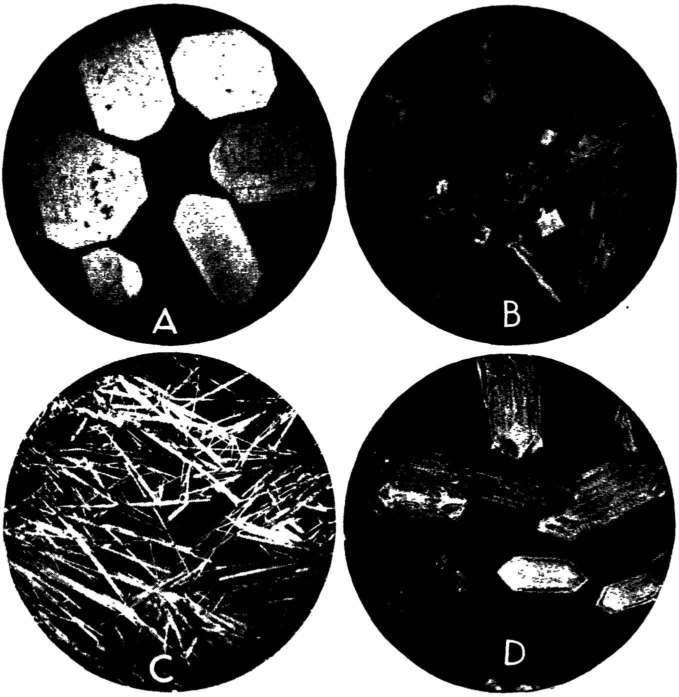


FIG. 177.—Coumarin. Type *A*, tabular crystals obtained by cooling melted coumarin to 67° to 69° C.; type *B*, aggregates of tabular crystals; type *C*, needles; type *D*, short prisms obtained from hot aqueous solutions.

The microchemistry of coumarin has been discussed in connection with vanillin (see pages 189, 190), for which it is occasionally found as a substitute. It may be readily obtained by microsublimation, usually occurring in prisms with oblique edges. With chlor-zinc-iodide, coumarin yields long, delicate, more or less bent, crystalline threads, brownish violet in color and tending toward clumping.

STANDARDS AND TESTS.—Coumarin should be free from vanillin and acetanilid (see National Formulary for tests).

Coumarin is rather widely distributed in Nature. Of the plants in which it has been found the following may be mentioned: vanilla grass or sweet vernal grass (*Anthoxanthum odoratum*); liatris, Carolina vanilla or deer's tongue (*Trilisa odoratissima*), one of the *Compositæ;* other species of *Melilotus*, as well as other genera of the *Leguminosæ;* sweet-scented bed straw (*Galium triflorum*), an herb of *Rubiaceæ* growing in the United States; the rhizomes of *Vitis sessilifolia* (*Vitaceæ*) of Brazil; and in *Prunus mahaleb* (Fam. *Rosaceæ*) of Europe.

Melilotus, Yellow Melilotus, or Yellow Sweet Clover (U. S. P. 1916 to 1926) is the dried leaves and flowering tops of *Melilotus officinalis* (Linné) Lamarck.

The plant is a biennial herb indigenous to Europe, but naturalized and cultivated in the United States. The stems are long, slender, straight, mostly simple and leafy below; leaves petiolate, trifoliate, stipulate, the leaflets 1 to 3 cm. in length; flowers in terminal racemes, yellow, 5 to 6 mm. in length, with papilionaceous corolla; legumes up to 3.5 mm. in length, obovate, wrinkled, one-seeded. Odor aromatic like coumarin; taste sweet, slightly pungent and bitter.

Melilotus contains coumarin, free or combined with melilotic acid; resins and a trace of volatile oil. The drug has been used as an antispasmodic and stimulant, and in resolvent plasters and poultices.

Trifolium, or Red Clover Blossoms (N. F. 1916 to 1947) is the dried inflorescence of *Trifolium pratense* Linné, a low-growing perennial herb, native to Europe, but naturalized in the United States and extensively cultivated for fodder.

DESCRIPTION.—Heads globose or ovoid, from 1.5 to 3 cm. in length, consisting of numerous purplish red or pinkish brown papilionaceous flowers, up to 15 mm. in length; calyx pubescent, and with subulate teeth shorter than the corolla; odor fragrant; taste somewhat sweetish and bitter.

CONSTITUENTS.—A volatile oil, coumaric acid, salicylic acid, myricyl alcohol, heptacosane, hentriacontane, sitosterol, isorhamnetin, together with several phenolic substances and glucosides, a mixture of fatty acids and a considerable quantity of sugar. Total ash, about 7.5 per cent; acid-insoluble ash, about 0.5 per cent.

USES AND DOSE.—Trifolium is an alterative and a sedative. Average dose, 4 gm.

Cascara Amarga, or Honduras Bark (N. F. 1926 to 1942) is the dried bark of *Sweetia panamensis* Benham. The name Cascara Amarga is from the Spanish meaning bitter bark. The plant is a tree indigenous to southern Mexico and Honduras. The dried bark is usually shipped in a matting wrapper.

Cascara amarga occurs in quills or in broken, irregular, flattened or transversely curved pieces up to 8 mm. thick; externally yellowish brown, more or less covered with grayish lichens showing blackish apothecia, or with cork more or less removed and reddish brown; inner surface grayish brown to dark reddish brown, with irregular longitudinal striations and numerous minute transverse markings; interior dark brown with a light yellow zone beneath the cork and numerous yellowish groups of stone cells; the latter especially pronounced in the older bark; fracture short, hard and brittle; odor faint; taste extremely bitter and persistent.

The powdered drug is light brown with numerous groups of bast fibers associated with crystal fibers, the latter with monoclinic prisms of calcium oxalate up to 40 microns in length; stone cells isolated or in large groups, the individual cells up to 100 microns in diameter; fragments of medullary ray tissue and parenchyma, the latter containing numerous irregular starch grains up to 25 microns in length, rarely larger, occasionally 2- to 4-compound; occasional fragments of brown cork; few slightly lignified or non-lignified fibers.

Cascara Amarga contains an alkaloid, picramnine, about 3 per cent; starch, about 2 per cent; total ash, 2.5 to 6.5 per cent, most of which is acid soluble.

Cascara Amarga is used as an alterative. Average dose, 1 gm.

ADULTERANTS.—A bark coming from the West Indies has been offered as cascara amarga or **West Indian Snake Root.** This bark does not resemble genuine cascara amarga in any respect. It is brownish black in color, about 2 mm. thick and usually in small broken pieces. Its botanical origin is not known. There has been much unintentional substitution of this drug for the genuine cascara amarga.

SENNA

Senna, or Senna Leaves (U. S. P. 1820 to date) consists of the dried leaflets of *Cassia acutifolia* Delile, known in commerce as **Alexandria**

Senna or *Cassia angustifolia* Vahl, known in commerce as **Tinnevelly Senna.** The name *Senna* is from *sena,* the native Arabian name of the drug; *Cassia* is from the Hebrew *qetsi-ah,* meaning to cut off, and refers to the fact that the bark of some of the species was once peeled off and used (the application of the name *cassia* to cinnamon barks should be noted); *acutifolia* is Latin referring to the sharply pointed leaflets and *angustifolia* means narrow-leaved. The plants are low-branching shrubs, *C. acutifolia* growing wild near the Nile River from Assouan to Kordofan; *C. angustifolia* growing wild in Somaliland, Arabia and India. Most of the commercial supply of the drug is collected from plants cultivated in southern India (Tinnevelly).

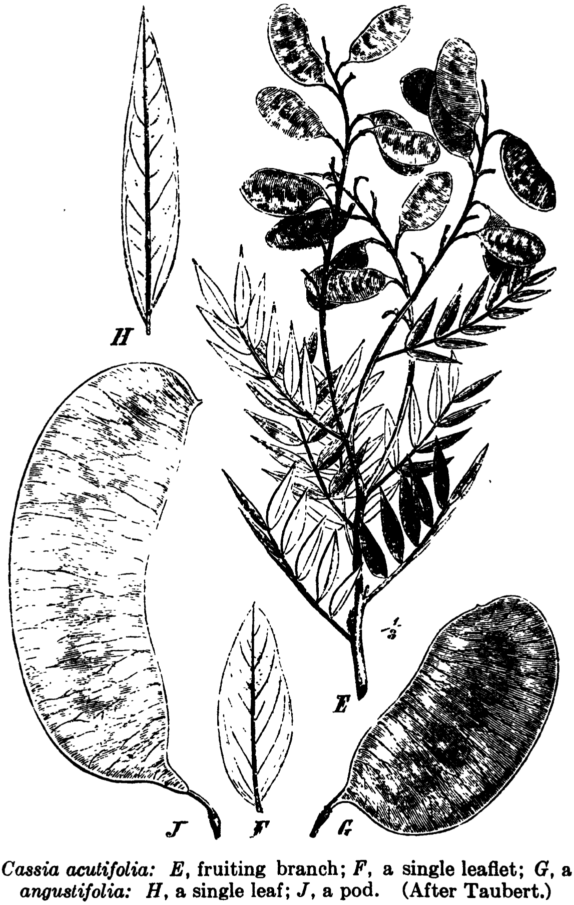


FIG. 178.—*Cassia acutifolia: E,* fruiting branch; *F,* a single leaflet; *G,* a pod. *Cassia angustifolia: H,* a single leaf; *J,* a pod. (After Taubert.)

Alexandria Senna is harvested in April and in September by cutting off the tops of the plants about 6 inches above the ground and drying them in the sun, after which the stems and pods are separated from the leaflets by means of sieves. That portion passing through the sieves is then "tossed," the leaves working to the surface and the heavier fragments of stalks sinking to the bottom. The leaves are then graded and baled or packed in bags and shipped via Alexandria and Red Sea ports. This process of collection and separation accounts for the large number of broken leaves in Alexandria Senna. Tinnevelly Senna is gathered by hand and dried in the sun, carefully baled and shipped via the ports

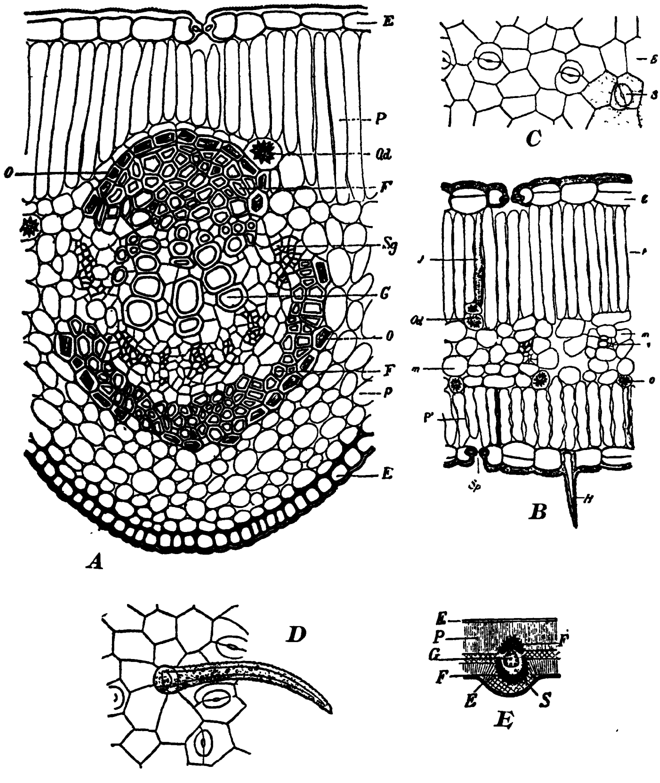


FIG. 179.—*Cassia angustifolia* (India Senna): *A*, transverse section through the middle vein showing upper epidermis (*E*), palisade cells (*P*), rosette aggregate of calcium oxalate (*Od*), monoclinic prisms of calcium oxalate (*o*), tracheæ (*G*), sieve (*Sg*), sclerenchymatous fibers (*F*), lower epidermis with rather thick-walled cells (*E*). *B*, transverse section through portion of leaf between the veins showing the absence of monoclinic prisms of calcium oxalate, the presence of palisade cells and stomata on both the lower and upper epidermis, and a hair (*H*) on the lower surface. *C*, lower epidermis in surface view. *D*, upper epidermis showing stomata and a single hair. *E*, diagram of section through the middle vein, the letters corresponding to those in *A*. (After Meyer.)

of Tuticorin, Madras and Calcutta. The Tinnevelly variety is more largely used, although the Alexandrian is said to be more highly esteemed. Senna was introduced into European medicine in the ninth or tenth century by the Arabians. Its native use seems to antedate historical record. According to Isaac Judæus, a native of Egypt who lived about 850–900 A.D., senna was brought to Egypt from Mecca.

DESCRIPTION, STRUCTURE, AND POWDER.—See Figures 178, 179, 180, and the U. S. Pharmacopœia.

CONSTITUENTS.—Senna contains one or more glycosides which yield hydroxymethylanthraquinone compounds, resembling those found in aloe and in rhubarb. The glycosides are not known in pure form but their derivatives by hydrolysis are well known, such as emodin, rhamnetin, chrysophanic acid, etc. The glycosides are readily soluble in water and the laxative strength of the drug is found in a well-prepared infusion of senna, or in the dried, powdered extract prepared from such an infusion. Liquid extracts of senna containing alcohol tend to precipitate the glycosides, and the supernatant portion of the extract becomes almost worthless. Highly concentrated preparations have been made that represent most of the laxation activity of the original drug, but only about 2 per cent of the weight of the drug; these probably approach closely to the pure glycosides.

STANDARDS AND TESTS.—Senna contains not more than 8 per cent of its stems, and not more than 2 per cent of its pods or other foreign organic matter, and yields not more than 3 per cent of acid-insoluble ash.

An assay for senna has been devised wherein the laxative effect upon mice of the unknown sample is compared to the laxative effect of the reference standard senna upon mice. A series of standard doses of each senna is injected into the stomachs of normal white mice of nearly uniform weight. The assay in full detail requires 200 mice. Each mouse is kept in a separate cage. After twelve to sixteen hours, the feces are noted. Non-laxation or laxation of different intensities can be readily distinguished on the blotting paper beneath each cage. A comparison is made between the action of the reference standard and that of the unknown sample and is expressed in percentage of the reference standard.

USES AND DOSE.—Senna is a laxative and a cathartic. Average laxative dose, 0.6 gm.

ADULTERANTS.—**Argel** leaves (*Solenostemma argel*, Fam. *Asclepidaceæ*) with non-glandular hairs 3- to 4-celled; **Coriaria** leaves (*Coriaria myrtifolia*, Fam. *Coriariaceæ*) poisonous, hence a dangerous adulterant; **Cracca** leaflets (*Tephrosia species*, Fam. *Leguminosæ*), also poisonous, are all adulterants that have been found in senna. Senna pods, excess stems, discolored leaflets, and especially dirt and sand, are frequently found in inferior grades of senna.

Senna Pods (Fig. 178), derived from both *C. acutifolia* and *C. angustifolia* are found in the market, sometimes admixed with senna leaflets; they are from 3.5 to 7 cm. in length and about 2 cm. in breadth, greenish brown to dark brown, and occasionally contain from 5 to 7 obovate, nearly smooth, dark brown seeds. The pods contain the same active principles as the leaflets, but in much less degree.

American Senna (U. S. P. 1820 to 1882) is the dried leaflets of *Cassia marilandica*, an herbaceous perennial, indigenous to the eastern and central United States and Canada, with 12- to 20-foliate leaves, yellow flowers and linear, slightly curved legumes. The laxative activity of the drug is very slight.

Cassia Obovata (U. S. P. 1831 to 1842) is the leaflets of *Cassia obovata* Linné. The leaflets are broad and obovate and the pods are distinctly curved. The plant is native to northern Africa and the leaflets are occasionally found in the official drug. They are not as laxative in action as the official senna.

Mecca Senna, or Arabian Senna, is obtained from wild plants of *C. angustifolia* growing in Arabia. **Aden Senna** is the leaflets of *C. holosericea*, of Abyssinia; they are quite hairy and are found occasionally in the market.

The leaves of other members of the *Leguminosæ* may be used like Senna, as *Cytisus purgans* of southern France, *Tephrosia apollinea* of Egypt, and *Colutea cruenta* of the Caucasus region.

The root of *Viviania esculenta* (Fam. *Geraniaceæ*), of the East Indies, contains a principle resembling cathartic acid.

Compound Senna Powder, or Compound Licorice Powder (U. S. P. 1828 to 1942; N. F. 1942 to date) consists of a mixture of powdered senna (180), powdered glycyrrhiza (236), washed sulfur (80), fennel oil (4), and powdered sucrose (500). The powder is weak yellow to dusky yellow in color with a fennel-like odor (see Fig. 180).

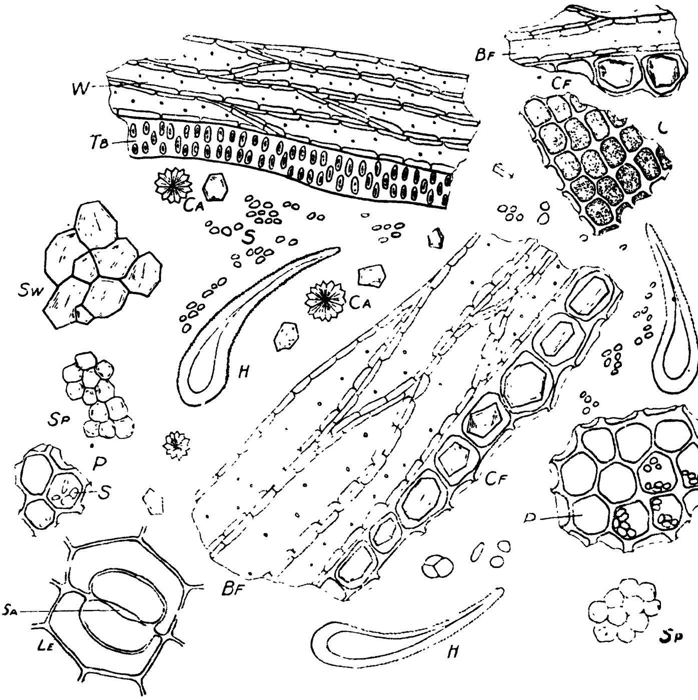


FIG. 180.—Compound Senna Powder. Fragments of Glycyrrhiza: *Bf*, bast fibers; *Cf*, crystal fibers; *W*, wood fibers; *Tb*, tracheæ having bordered pores; *C*, cork cells, filled with a reddish brown amorphous content; *Ca*, monoclinic prisms of calcium oxalate from 10 to 30 microns in length; *P*, parenchyma cells containing starch grains (*S*), from 2 to 20 microns in diameter. Fragments of Senna: *H*, non-glandular hairs with papillose walls; *Le*, fragment of lower epidermis showing a stoma (*Sa*); *Ca*, rosette aggregates of calcium oxalate 10 to 20 microns in diameter. Fragments of Sulfur: *Sw*, aggregates of angular fragments of washed sulfur; *Sp*, aggregates of spheroidal fragments of precipitated sulfur. (Drawing by Hasse.)

DESCRIPTION AND TESTS.—When mounted in a fixed oil and examined under the petrographic microscope it shows a large number of irregular, angular fragments of sugar, which polarize light strongly and are furthermore readily soluble in mounts made with water; upon the addition of solutions of potassium hydroxide to aqueous mounts of the powder, the fragments of senna are immediately colored a yellowish red, changing to a reddish brown. On moistening 0.1 gm. of the powder with 2 cc. of alcohol, adding 10 cc. of water and boiling, then cooling and filtering, the filtrate should be of a pale yellowish brown color, which, upon the addition of a drop of solution of potassium hydroxide, changes to a yellowish red.

USES AND DOSE.—Compound Senna Powder is a laxative and a cathartic. Average dose, 4 gm.

COPAIBA

Copaiba, or Balsam Copaiba (U. S. P. 1820 to 1942; N. F. 1942 to date) is an oleoresin derived from South American species of *Copaifera* (*Copaiba*). *Copaiba* is from the Brazilian native name *cupauba.* The plant is a tree up to 18 meters in height. The oleoresin, which is a physiological product, is formed in schizolysigenous cavities in the wood and seems to be a metamorphosed product of the cell walls; these cavities sometimes contain several liters of the oleoresin. The trees are tapped or boxed (see Turpentine) to the center of the tree and the oleoresin conducted directly to containers. A tree frequently yields 20 to 24 liters.

There is considerable variation in South American copaiba from different sources. The two principal varieties are: (1) **Para or Maranham copaiba** from *Copaiba langsdorfii* and *Copaiba coriacea,* which is optically levogyrate; (2) **Maracaibo or Venezuela copaiba,** obtained from *Copaiba officinalis* and *Copaiba guyanensis* which is more viscid, darker in color and dextrogyrate.

The first description of the collection of copaiba is that of Marcgrav and Piso (1648), although Petrus Martys mentions the *copei* tree as early as 1534.

It should be noted that the term *balsam* is erroneously applied Copaiba is an oleoresin and contains neither benzoic nor cinnamic acid.

Description.—A pale yellow to yellowish brown, viscid liquid, more or less transparent and highly refractive, sometimes slightly fluorescent, having a distinct aromatic odor and a bitter, acrid, persistent taste. It is soluble in absolute alcohol, chloroform, ether and carbon disulfide.

Constituents.—Volatile oil, resin acids, and a small quantity of a bitter principle.

Standards and Tests.—See the National Formulary.

Uses and Dose.—Copaiba is a genito-urinary disinfectant. It is a diuretic, a stimulant, an expectorant, and a laxative. Average dose, 1 cc.

Adulterants.—Oil of turpentine, liquid paraffin, castor oil, olive oil, rosin, gurjun balsam and African copaiba have been found admixed with copaiba and may be detected by the pharmacopœial tests.

Copaiba Oil (U. S. P. 1851 to 1916) is obtained by direct distillation of copaiba. The yield is from 35 to 70 per cent, higher from Para than from Maracaibo copaiba. When fresh it is a colorless liquid, but on standing becomes yellow to greenish yellow, with the odor of copaiba and a pungent taste. It is easily soluble in alcohol, ether or carbon disulfide. It is levorotatory (−7° to −35°). It consists chiefly of caryophyllene.

In medicinal activity it represents most of the value of copaiba.

Copaiba Resin (U. S. P. 1882 to 1905) is the residue remaining after distilling off the volatile oil of copaiba. It consists largely of several resin acids: metacopaivic and illuric (illurinic) in Maracaibo copaiba; copaivic and oxycopaivic in Para copaiba. It is yellowish brown to dark brown in color; insoluble in water, but slightly soluble in alcohol and readily soluble in the other usual volatile solvents. The resin possesses but little medicinal value.

Gurjun Balsam is an oleoresin yielded by various species of *Dipterocarpus* (Fam. *Dipterocarpaceæ*) native to India, Siam and other countries of southern Asia. It is less acrid than copaiba.

African Copaiba is probably derived from *Hardwickia* sp. Its oil is dextrorotatory (+5° to +30°).

Copal is a fossil resin or is found exuding from various leguminous plants. Its medicinal properties resemble those of copaiba but it finds its principal usage in the manufacture of varnishes.

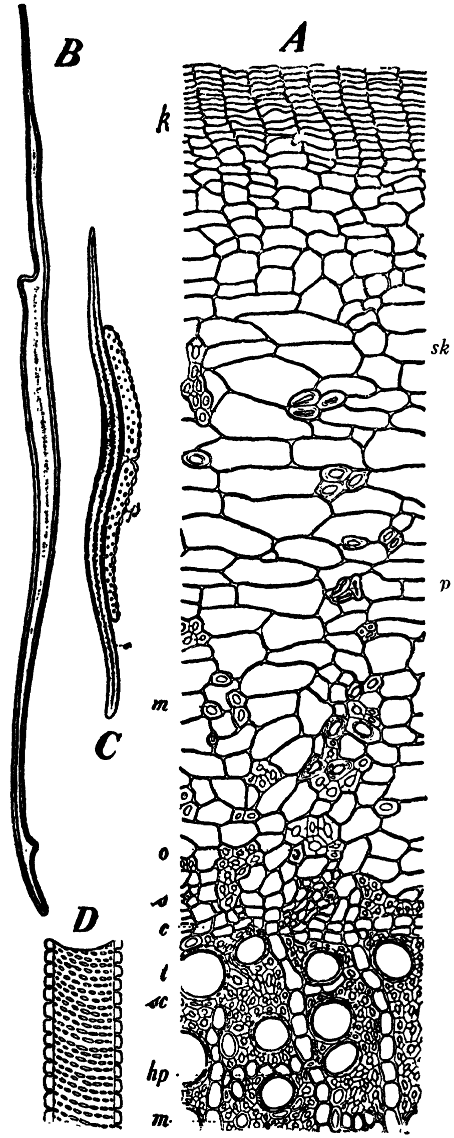


Fig. 181.—Peruvian Rhatany: *A*, transverse section showing cork (*k*), a group of bast fibers (*sk*), parenchyma of cortex (*p*), medullary-ray cells of inner bark (*m*), cambium (*c*), tracheæ (*t*), wood fibers (*sc*), wood parenchyma (*hp*), medullary rays one cell in width (*m*); *B*, an isolated bast fiber; *C*, a wood fiber with neighboring parenchyma cells which are somewhat elongated and have somewhat thickened, porous walls; *D*, portion of a trachea. (After Meyer.)

Damar, Dammar, or Resin Damar as a mounting medium (N. F. 1942 to date) is the resinous exudate from *Shorea Wiesneri* Schiffner (Fam. *Dipterocarpaceæ*).

This tree is native to Australasia, East Indies and the Philippines where the exudate is collected. The resin is in yellowish, rounded or irregular, friable masses, semi-transparent and melting about 120°. It is insoluble in water, moderately soluble in alcohol and readily soluble in chloroform, ether, carbon disulfide and xylene. Its principal use is in varnishes and lacquers, occasionally in medicinal plasters. A filtered solution in xylene, concentrated to a suitable consistency, is used for mounting microscopic specimens.

Krameria, or Rhatany (U. S. P. 1831 to 1916, 1926 to 1936; N. F. 1916 to 1926, 1936 to 1947) is the dried root of *Krameria triandra* Ruiz et Pavon, known in commerce as Peruvian Rhatany; or of *Kramaria Argentea* Martius (1894 to 1947), known in commerce as Para or Brazilian Rhatany; or of *Krameria tomentosa* Saint Hilaire (*K. Ixina* Linné), known in commerce as Savanilla Rhatany (1882 to 1926). *Kramaria* was given in honor of J. G. H. and W. H. Kramer, two eighteenth century German botanists; *triandra* is Latin, meaning three stamens, and *argentea* refers to the silvery appearance of the leaves.

The plants are low shrubs with spreading branches. *Krameria triandra* grows on the sandy slopes of the Bolivian and Peruvian Cordilleras, and *Krameria argentea* is found mostly in Brazil, being shipped from Para or Rio de Janeiro; *Savanilla rhatany* is produced in Colombia, British Guiana and northern Brazil. The Spanish botanist Hipolito Ruiz (1784) observed the native women of Lima using the drug as a tooth preservative and astringent. He introduced it into Spain, from which its use gradually spread through Europe.

The root crown is knotty, several to many-headed, with numerous branching roots not more than 1 cm. in thickness; roots are cylindrical or tapering (Para), flexuous or wavy; Peruvian rhatany is dusky red to moderate brown, considerably marked with scaly cork and devoid of transverse fissures; Para rhatany is darker in color and marked with numerous fissures. The bark of Peruvian Rhatany is about one-third of the diameter of the root; that of Para about one-half; the wood is orange color, the bark dark red. For structure see Figure 181.

Powdered krameria is moderate brown, inodorous and very astringent; starch grains are simple or few-compound, usually with a central cleft and up to 35 microns in diameter; calcium oxalate in prisms up to 100 microns long and occasional microcrystals; bast fibers long, wavy, much attenuated, and non-lignified; wood fibers numerous, spindle-shaped, thick-walled, but only slightly lignified; tracheæ with simple or bordered pores. (See Fig. 181.)

Krameria contains from 8 to 20 per cent of tannin; krameric acid; starch; an uncrystallizable sugar; and calcium oxalate. The tannin is a phlobotannin and is colored dark green with solutions of ferric salts; it forms the phlobophene krameria-red and upon further decomposition yields phloroglucin and protocatechuic acid. Total ash, about 2 per cent; acid-insoluble ash, about 0.25 per cent.

Krameria more than 1 cm. in thickness should be rejected.

Krameria is an astringent and a tonic. Average dose, 1 gm.

Krameria lanceolata of the southern United States furnishes the **Texas Krameria,** and *K. cistoides* of Chile is the source of the **Payta Krameria.** The root of *Leea speciosa* (Fam. *Vitaceæ*) of India has been used as a substitute for krameria.

ACACIA

Acacia or Gum Arabic (U. S. P. 1820 to date) is the dried gummy exudation from the stems and branches of *Acacia senegal* (Linné) Willdenow, or of some other African species of *Acacia*. *Acacia* is the

Greek *akakia,* coming from *ake,* meaning pointed and referring to the thorny nature of the plant; *senegal* refers to its habitat. The name "gum arabic" seems to be a misnomer, since very little acacia is produced in Arabia and none is exported. It may have had its origin in the fact that the drug was extensively used by the early Arabian physicians.

Acacia plants are thorny trees about 6 meters in height growing in Kordofan in the Anglo-Egyptian Sudan and in Senegambia (Senegal). Most of the official drug comes from cultivated trees in Kordofan. The trees are tapped by making a transverse incision in the bark, peeling the bark both above and below the cut, thus exposing an area of cambium 2 to 3 feet in length and 2 to 3 inches in breadth. In two or three weeks the tears of gum formed on this exposed surface may be collected. The formation of the gum may be due to bacterial action or to the action of a ferment. No trace of metamorphosed cell walls are found in the gum, therefore it must be formed from cell contents. The gum is occasionally exposed to the sun to bleach it. Numerous minute cracks often form in the outer portion of the tears during the bleaching process, thus giving them a semi-opaque appearance. The tears are garbled and graded by hand, then packed and shipped via Port Sudan. Acacia has been an article of commerce since most remote times. The tree, together with heaps of gum, is pictured during the reign of Rameses III, and in later inscriptions. It was exported from the Gulf of Aden seventeen hundred years before Christ. Theophrastus mentions it in the third century B.C. under the name of "Egyptian Gum." During the Middle Ages it was obtained from Egypt and Turkey. The west African gum (Senegal) was imported by the Portuguese during the fifteenth century.

DESCRIPTION.—In spheroidal tears or angular fragments of variable size; externally whitish or yellowish white with numerous minute fissures; translucent; very brittle, with a glass-like sometimes iridescent fracture; nearly inodorous; taste mucilaginous. Acacia is insoluble in alcohol but almost completely soluble in twice its weight of water.

POWDER.—Oyster-white; soluble in cold water, forming a sticky paste and containing few or no altered or unaltered starch grains or vegetable tissues.

CONSTITUENTS.—Acacia consists principally of arabin which is composed of arabic acid in combination with calcium and traces of potassium and magnesium. Mild hydrolysis of arabic acid yields l-arabinose, l-rhamnose and 3-d-galactoside-l-arabinose. The residue is composed of galactose and glucuronic units in the proportion of 3 to 1. Methylation experiments indicate that the stable nucleus is composed of nine galactose residues and three glucuronic residues, so linked as to give a branched chain structure having four terminal or end residues but only one reducing group. These terminal residues are composed of uronic groups and galactose in the ratio of three to one. Acacia also contains an oxydase and from 12 to 15 per cent of water.

STANDARDS AND TESTS.—Acacia yields not more than 1 per cent of water-insoluble residue, not more than 4 per cent of total ash, not more than 0.5 per cent of acid-insoluble ash, and not more than 15 per cent of moisture. The addition of 0.2 cc. of diluted lead subacetate solution to 10 cc. of a 2 per cent cold aqueous solution of acacia immediately produces a flocculent, curdy white precipitate. A 10 per cent aqueous solution of acacia should show but slight levorotation. One-tenth cubic centimeter of ferric chloride T.S. added to 10 cc. of a 2 per cent aqueous solution of acacia should show no blackish coloration nor blackish precipitate (tannin-bearing gums). Iodine T.S. added to a 2 per cent aqueous solution of acacia which has been previously boiled and cooled should produce no bluish or reddish color (starch or dextrin).

USES.—Acacia is a demulcent. It is used also as an emulsifying agent and in making mucilage.

ADULTERANTS.—An artificial gum has been prepared by heating starch with sulfuric acid in an autoclave, the resulting product being neutralized, washed and then dried. It is said to resemble acacia in appearance and adhesiveness.

The powder, while sometimes adulterated with dextrin and rice starch, is more frequently mixed with inferior gums, especially the mesquite gum.

ALLIED PLANTS.—Gums with a brown or red color are obtained from *A. arabica*, *A. seyal*, *A. stenocarpa* and *A. ehrenbergiana*. There are a number of gums which have many of the properties of gum arabic; as **Cape Gum,** from *A. horrida* and *A. giraffæ;* **Australian or Wattle Gum,** from the golden wattle (*A. pycnantha*), or tan wattle (*A. decurrens* and *A. homalophylla*).

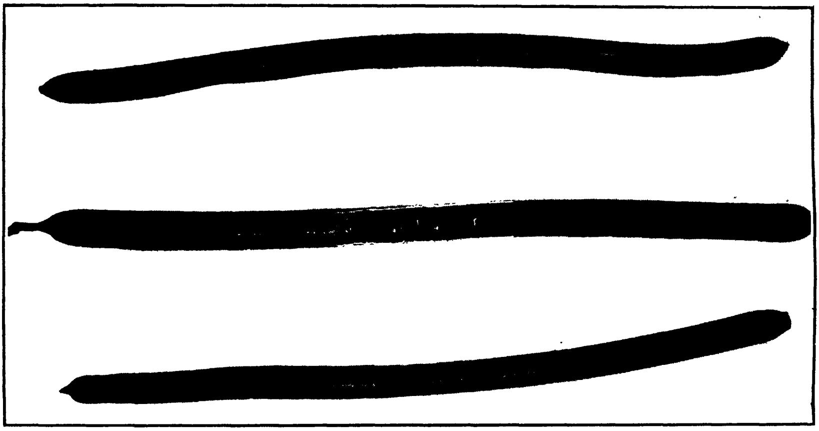


FIG. 182.—Cassia Fistula × $\frac{1}{5}$: the middle fruit is partially cut away to show the transverse partitions and seeds. (Photo by Adamson.)

Mesquite Gum is obtained from *Prosopis juliflora*, of the southern United States and Mexico. The tears are nearly smooth, light yellowish brown to dark brown, more or less opaque, but translucent and glassy when fractured. The powder is of a whitish or grayish white color. The gum is further distinguished by not giving precipitates with solutions of lead subacetate, ferric chloride and sodium borate. Mesquite forms a somewhat adhesive mucilage and can be used as an emulsifying agent.

Ghatti Gum or Indian Gum is an exudation from the wood of *Anogeissus latifolia* (Fam. *Combretaceæ*), a tree indigenous to India and Ceylon. It occurs in yellowish white tears with a dull, rough surface and a vitreous fracture. It is entirely soluble in cold water, forming a very viscous mucilage. A 1 per cent solution of Ghatti gum gives a precipitate with a 10 per cent tannic acid solution. This is a distinction from acacia.

CASSIA FISTULA AND TAMARIND

Cassia Fistula, or Purging Cassia (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the dried fruit of *Cassia* (*Cathartocarpus* Persoon) *Fistula* Linné, a tree indigenous to India and naturalized in tropical Africa, Java, South America and the West Indies.

Cassia Fistula Pulp also was recognized in the U. S. P. 1831 to 1863.

The legume is nearly straight, indehiscent, cylindrical, 25 to 50 cm. in length, 15 to 20 mm. in diameter; externally reddish brown, the apex acute or acuminate, the base rounded and sometimes with a woody pedicel; smooth, shiny, transversely striate, on one side with a longitudinal groove (the ventral suture); pericarp hard and woody; internally divided by transverse partitions into numerous compartments about 5 mm. in length, each containing brownish black pulp and a single seed; the odor of the pulp is distinct, prune-like and the taste sweet. The fruit yields about 30 per cent of pulp, which contains 40 to 60 per cent of sugar. The drug is a laxative or purgative but apparently does not owe its laxative properties to any of the anthraquinone derivatives found in senna and related plants.

Tamarind (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the partially dried, ripe fruit of *Tamarindus indica* Linné, deprived of the brittle outer portion of the pericarp and preserved in sugar or syrup.

Tamarind Pulp also was recognized in the U. S. P. 1831 to 1863.

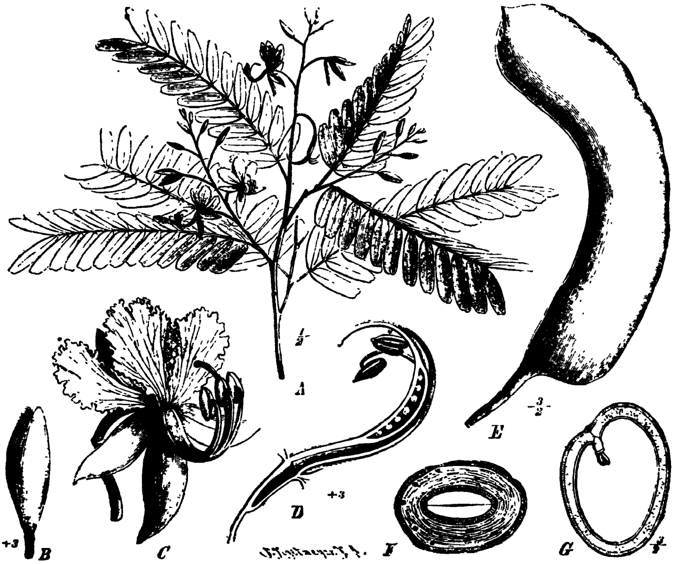


FIG. 183.—*Tamarindus indica: A*, flowering branch with paripinnate leaves; *B*, flower bud; *C*, dorsiventral (irregular) flower; *D*, longitudinal section of flower showing unilocular ovary; *E*, somewhat curved, indehiscent legume; *F*, *G*, transverse and longitudinal sections of the seed. (After Taubert.)

The tamarind tree is indigenous to Africa and is cultivated in the West and East Indies, whence the two chief commercial varieties are obtained. In the West Indies, the epicarps are removed from the legumes and boiling syrup is poured over the pulp and seeds, while in the East Indies the pulp is worked up into a mass with sugar. The product is often marketed in earthenware vessels of about 1 pound capacity.

West Indian tamarind is usually a blackish brown mass, with a distinct odor and a strongly acidulous, sweet taste, in which are embedded numerous seeds enclosed in a loose, tough membrane.

East Indian tamarind occurs in blackish cakes, containing less sugar and more acids.

Tamarind contains tartaric, citric and malic acids (10 to 20 per cent); organic acid salts; invert sugar, 32 to 42 per cent; total ash about 3.6 per cent; acid insoluble ash about 0.25 per cent. The drug is used as a mild laxative and refrigerant.

PEANUT

Peanuts are the ripe fruit or seed of *Arachis hypogæa* Linné. The plant is a low annual herb with imparipinnate leaves and yellow papilonaceous flowers; it is native to Brazil but is extensively cultivated in the southern United States, China and other semi-tropical localities. The fruit is not a true nut, but the immature pod penetrates into the soil and the fruit ripens underground. It contains from 1 to 6 reddish brown seeds.

The green tops of the plants form an excellent hay, **Peanut Hay,** but when the fruits are fully ripened, the value of the hay is much reduced. When ripe the plants are raked from the soil with the fruits into windrows. When dry the pods are machine-separated and sacked for shipment; or the dried plants are threshed to separate and clean the seed. For human consumption the fruit are roasted, then passed between rollers and the seed are separated. The kernels contain about 45 per cent of fixed oil, 20 per cent of protein and a high content of thiamine, hence they are highly nutritious, and are extensively used as food, both whole, and when reduced to a paste, as **Peanut Butter.**

Peanut Oil (U. S. P. 1947 to date) is the fixed oil obtained by cold pressure from the peeled ripe seed of one or more of the cultivated varieties of *Arachis hypogæa* Linné.

Peanut Oil is a yellowish liquid with a slight nut-like odor and a bland taste. For constants and tests of identity and purity, see the U. S. Pharmacopœia.

Peanut oil consists chiefly of olein with small percentages of several other glycerides. It closely resembles olive oil and the Pharmacopœia permits its use in liniments, ointments, plasters and soaps in place of olive oil. Its principal use is as a food oil. It is a non-drying oil, hence has no value in paints, but is a valuable lubricant. The oil saponifies slowly, but yields an excellent, firm, white soap.

Peanut Oil Cake is a valuable stock food.

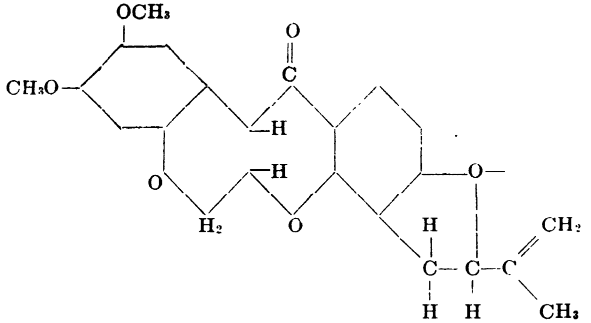
ROTENONE

Rotenone is one of the insecticidal principles obtained from the root of *Derris elliptica* Bentham, *Derris malaccensis* Bentham, *Derris negrensis, Lonchocarpus nicou* DC, *Lonchocarpus utilis* Kleinh., *Lonchocarpus chrysophyllus* Kleinh., *Tephrosia toxicaria, Tephrosia virginiana* Linné, or other species of *Derris, Lonchocarpus* or *Tephrosia.*

Derris Root or Tuba Root appears in commerce from British Malaya, the Netherlands Indies and the Philippines, mostly from cultivated plants. About 2.5 million pounds of derris root were imported into the United States in 1939. The genus *Lonchocarpus* includes several trees and shrubs growing in Mexico, Central and South America, and to a limited extent in Africa and Australia. The commercial root is known as **Cube Root** (pronounced Koo-bay) or that from Amazonian Brazil as **Timbo Root.** About 2 million pounds were imported in 1939. The genus *Tephrosia* is widely distributed over most of the world. Of recent interest, is the **Devil's Shoestring** (*Tephrosia virginiana*) growing in the eastern and southern United States.

These roots may contain rotenone, deguelin, toxicarol or tephrosin, compounds structurally related, and having insecticidal properties. The roots are usually assayed both for rotenone content and for ether-soluble or for acetone-soluble extractive, which represents all of the insecticidal principles that may be present. Cultivated *Derris elliptica* root may contain 13 per cent of rotenone or 30 per cent of ether-soluble extractive; Philippine derris contains 4 to 5 per cent of rotenone, and *Lonchocarpus* species yield 8 to 10 per cent of rotenone; *Tephrosia* species contain about 0.5 per cent of rotenone.

Rotenone is extracted by means of suitable organic solvents, and crystallized. It is a white, odorless compound having the following formula:



and crystallizes from alcohol in six-sided orthorhombic plates. Its melting point is 163° C. and its solutions are levorotatory; it is soluble in most organic solvents except carbon tetrachloride, slightly in the petroleum oils, and insoluble in water.

Rotenone is used to a limited extent in pharmaceutical preparations used on the skin (powders, ointments, etc.), where its action is that of an insecticide. With the discovery of DDT, however, this use diminished to a considerable extent. Rotenone is used as a general insecticide in sprays or dusts. The commercial dusting powders may contain pure rotenone, acetone extract or the powdered roots admixed with kaolin, talc, clays, ground walnut shell or other inert material so as to contain a concentration of rotenone of about 1 per cent.

Rotenone is exceedingly poisonous to insects and to fish but is practically harmless to higher animals. Goldfish die in water containing 1 part of rotenone in 20 million parts of water, but the lethal oral dose for dogs is 300 mg. per kilo of weight. Rotenone dusts are therefore quite safe for dusting drug plant crops as well as vegetable crops.

HEMATOXYLON

Hematoxylon or Logwood (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the heartwood of *Hæmatoxylon campechianum* Linné, a tree indigenous to Central America and naturalized in the West Indies. The bark and colorless sapwood are removed and the heartwood is cut into logs for the market.

The drug usually occurs in small chips, reddish brown externally, the freshly cut surface dark yellowish red; in transverse section radiate, and with numerous alternate, yellowish and reddish concentric rings; hard, fibrous; odor slight; taste sweet, astringent; the wood imparts to water a violet or wine color. The wood contains much tannin (gallotannin), some resin and hematoxylin. The drug has been used as an astringent.

Hematoxylin (U. S. P. 1905 to 1926; 1936 to date; N. F. 1926 to date) is in colorless or pale yellow prisms, and present in logwood to the extent of 10 to 12 per cent. It is sparingly soluble in water, readily soluble in hot water and in alcohol. It is used as an indicator, a stain for microscopic sections, and in the manufacture of inks and dyes.

Hematein (U. S. P. 1916 to date; N. F. 1936 to date) is an oxidation product of hematoxylin. It forms in the wood on exposure to air so that the chips become dark red and have a greenish metallic luster. It forms rapidly when hematoxylin is dissolved in alkaline (ammonia) solutions.

It occurs as yellowish brown crystals with a yellowish green metallic luster. It is insoluble in water, alcohol, chloroform, or ether, but dissolves in alkaline solutions with a red color. It is used as an indicator and in nuclear stain for cytologic sections.

Fermented (oxidized) logwood has an extensive use as a textile dye. Note that the dye value of each of the above logwood products is due to the hematein.

Brazil Wood (U. S. P. 1894 to 1916) is obtained from *Cæsalpinia echinata* Lamarck, and contains the principle known as **brazilin,** which is colorless when first extracted, but assumes a red color on exposure to the air. It was used as an indicator in the Pharmacopœia.

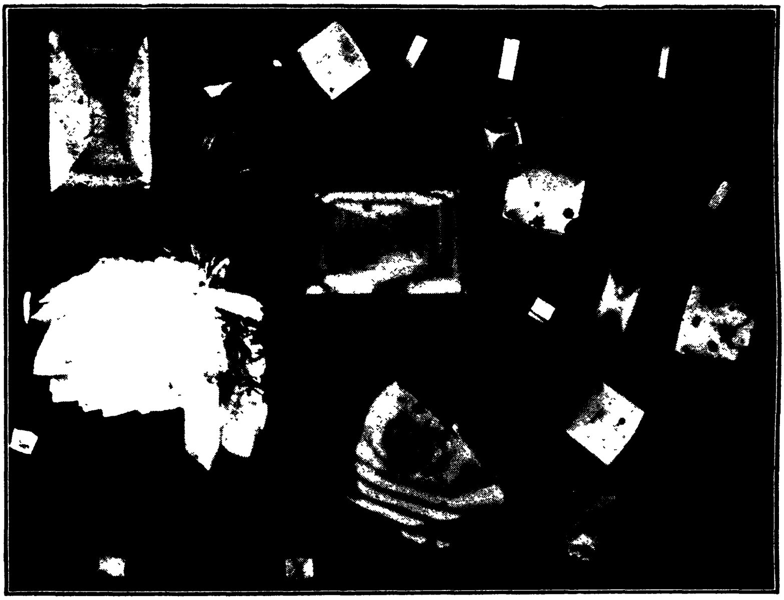


FIG. 184.—Hematoxylin: monoclinic tabular crystals from aqueous solution.

Sappan or False Sandalwood is obtained from *Cæsalpinia Sappan* Linné of Indo-China; it contains brazilin and is used as a dye-wood and an indicator as is brazil wood. Red coloring principles are also found in other species of *Cæsalpinia* and in other genera of the *Leguminosæ.*

SOY BEAN

Soy Bean is the ripe seed of *Glycine Soja* Sieb. et Zucc., an important food and forage crop. The plant is an annual with trifoliate, hairy leaves; rather inconspicuous, pale blue to violet-colored flowers; and broad pods containing 2 to 5 seeds. The seeds are more or less compressed, spheroidal or ellipsoidal and vary in color from nearly white to yellow-green or brownish black. The seed contain about 35 per cent of carbohydrates, up to 50 per cent of protein substances, up to 20 per cent of fixed oil, and the enzyme urease.

Soy beans are used medicinally as a food for diabetics, and, especially in China, as a general food for humans and stock. **Soy Bean Hay** is a valuable stock food.

Soy Bean Meal, as a reagent (N. F. 1942 to date) is the flour sifted from the decorticated, ground seed of *Glycine Soja,* deprived of fat. It is used for the detection of urea nitrogen in blood serum by the enzymatic action of the urease in the soy bean meal.

Soy Bean Oil is obtained by pressure, the yield seldom exceeding 10 per cent. The oil contains 50 per cent or more of linolic acid and considerable linolenic acid, hence it is a drying oil and not useful as a food oil. It is extensively used in the manufacture of varnishes, insulators, etc.

Soy Bean Cake, the residue after pressing out the oil, has a high value as a stock food. It not only contains a large amount of protein and some oil, but the 5 per cent of ash consists largely of potassium and phosphorus. Fiber is but 2 to 5 per cent.

Baptisia, or Wild Indigo Root (U. S. P. 1831 to 1842; N. F. 1916 to 1936) is the dried root of *Baptisia tinctoria,* a perennial herb growing in the eastern United States and Canada. The drug is gathered in the fall, and consists of a warty crown, branching into stem remnants and buds, and bearing numerous roots which are 0.5 to 4 cm. in thickness, externally brown, longitudinally wrinkled, occasionally spirally twisted, somewhat scaly, and with long, wiry, somewhat branching rootlets; the fracture is short and fibrous; the inner surface is whitish, and the bark is thick and easily separable from the porous radiate wood; the odor is distinct and the taste of the bark is bitter and slightly acrid.

Baptisia contains a crystalline alkaloid, cytisine (baptitoxine), which is very soluble in water and alcohol and is almost insoluble in ether and chloroform. It also contains baptin, which forms acicular crystals and is purgative; and about 6 per cent of baptisin, a crystalline glucoside. Total ash about 2.5 per cent; acid-insoluble ash about 0.5 per cent.

In large doses it is an emetic and cathartic.

Galega, or European Goat's Rue (N. F. 1916 to 1936) is the dried flowering tops of *Galega officinalis,* a perennial herb common in southern Europe and cultivated to some extent. The tops are gathered in July and August, at the time of the flowering of the plant, and carefully dried.

The stem is cylindrical, hollow, from 2 to 3 mm. in diameter, pale green or greenish brown, distinctly longitudinally ribbed or furrowed; the leaves are odd-pinnate, the leaflets nearly sessile, elliptical, entire and mucronate-tipped, from 10 to 40 mm. in length and from 5 to 12 mm. in width, of a light green or greenish brown color, nearly glabrous; the flowers are about 15 mm. in length, white or violet-blue and borne in racemes; the odor is slight and the taste slightly bitter.

Galega contains a bitter principle and tannic acid. Total ash about 10 per cent; acid-insoluble ash about 0.5 per cent.

Galega is claimed to be a galactagogue. It is a mild astringent and a tonic.

Cowhage, Dolichos, or Mucuna (U. S. P. 1820 to 1882) consists of the hairs of the pods of *Mucuna pruriens,* a climbing plant growing in the East and West Indies. The hairs are about 3 mm. long, sharply pointed and somewhat serrate on the upper half. They easily penetrate the skin, and occasion an intolerable itching, which is greatly increased by washing and rubbing. It has been employed as an anthelmintic.

Catechu, Black Catechu, or Black Cutch (U. S. P. 1820 to 1905) is an extract prepared from the heartwood of *Acacia catechu,* a tree indigenous to India and Burma. The wood is extracted with boiling water, the extract strained, evaporated to a syrupy consistency and allowed to harden. The drug occurs in irregular masses, with fragments of leaves or mats upon the outside; it is reddish black, somewhat shiny, brittle, more or less porous, and has a slight odor and an astringent and sweetish taste. It contains about 25 per cent of phlobatannin called catechutannic acid and is used as an astringent.

Black catechu is also extracted from the wood of *Acacia suma,* of India. The barks of a number of species of *Acacia* growing in Australia, and known as wattle barks, are used in the preparation of an extract resembling black catechu. The tannin of *Acacia arabica* and of several species of *Cæsalpinia* yield on hydrolysis gallic and ellagic acids.

A tannin resembling catechu is obtained from the bark of *Eugenia smithii* (Fam. *Myrtaceæ*) of Australia. A catechu-like extract is obtained from the bark of the Mahogany Tree (*Swietenia mahogoni*), one of the *Meliaceæ* of the West Indies and Central America.

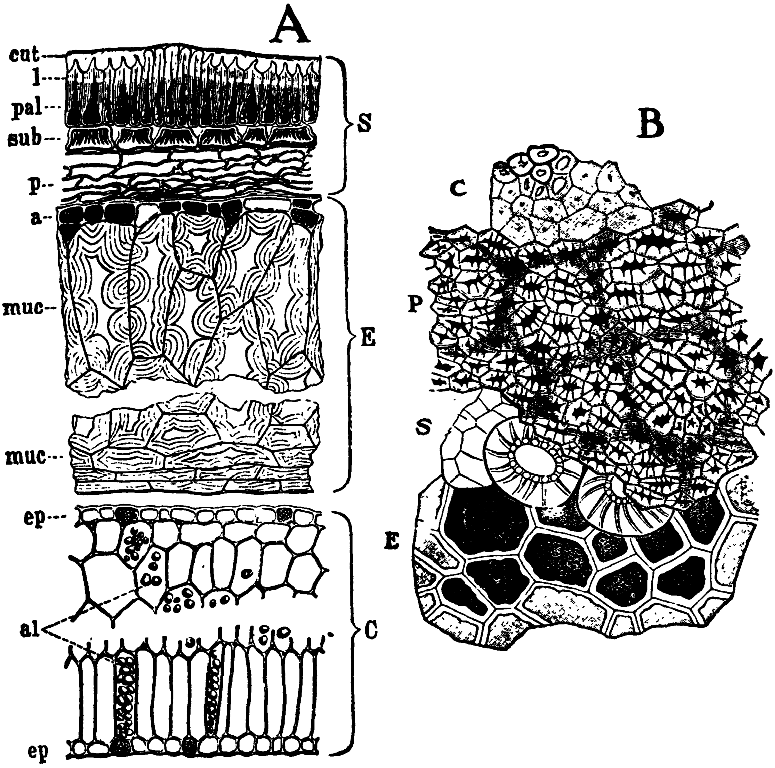


FIG. 185.—Fenugreek: *A*, transverse section of seed: *S*, testa or seed coat consisting of palisade cells (*pal*), with thick cuticle (*cut*) and thick lamellated walls (*l*); hour-glass-shaped column cells (*sub*); and parenchyma (*p*); *E*, endosperm layer consisting of cells containing small aleurone grains (*a*); and thick-walled mucilage cells (*muc*); *C*, tissues of cotyledon consisting of the two epidermal layers (*ep*) and cells containing small aleurone grains (*al*). *B*, Surface sections of tissues of the seed coat and endosperm: *C*, cuticle and palisade cells with small lumina; *P*, palisade cells with thick radiating porous walls and large lumina; *S*, subepidermal or column cells and parenchyma; *E*, cells of endosperm containing aleurone grains (*A*, after Winton; *B*, after Tschirch).

Mangrove Extract is prepared from the bark of the red variety of *Rhizophora mangle* or *R. mucronata* (Fam. *Rhizophoraceæ*) and contains about 70 per cent of tannic acid. It is sometimes sold as catechu. It gives a green precipitate with solutions of ferric salts; a reddish black color with a solution of copper sulfate and ammonia; a reddish brown color with sulfuric acid; a reddish precipitate with lime water, darkened by excess; and a slight reddening with a solution of stannous chloride and hydrochloric acid. It apparently belongs to the same class of tannins as hemlock, oak, rhatany and canaigre.

Fenugreek is the dried ripe seed of *Trigonella fœnum-græcum*, an annual herb indigenous to the Mediterranean region and extensively cultivated in southern Europe, northern Africa and India.

The seeds are oblong-flattened or rhomboidal; from 3 to 5 mm. in length; externally light to dark yellowish brown; hard, heavy, and pebble-like; the odor is distinct, resembling that of elm bark, and the taste mucilaginous and slightly bitter.

The structure is shown in Figure 185.

Fenugreek contains about 50 per cent of proteins and mucilage but no starch. It is extensively used as a nutrient for stock. Medicinally, it is used as a demulcent and emollient, usually in combination with other remedies, and especially in veterinary medicine.

Alfalfa is the overground portion of *Medicago sativa* and is extensively cultivated as a cattle food. **Alfalfa Hay** when well dried and ground to a fine powder constitutes **Alfalfa Meal,** which is used to some extent in human food and very extensively in mixed feeds for cattle and fowl. The plant is rich in proteins and certain vitamins.

Abrus, Jequirity or Wild Liquorice Seed is the seed of *Abrus precatorius*, a climbing shrub common to tropical and subtropical countries of both hemispheres. *Abrus* is from a Greek word meaning graceful, in allusion to the flowers; *precatorius* is derived from the Latin *precor*, meaning to pray, because the seeds are used as beads in rosaries. The seeds are ovoid, globular, from 5 to 9 mm. in length, hard, smooth and shining, of two distinct colors, the lower or hilum portion scarlet red and with a large lenticular scar; the upper portion purplish black; testa, shell-like and enclosing a light yellowish brown embryo having two large cotyledons and an incurved radicle. The seed contains abrin (jequiritin), an agglutinating, phytalbumose, resembling ricin in its physiological action. It is very toxic, is soluble in a solution of sodium chloride and decomposes upon heating to 85° C. Recent researches show it to be composed of abrusalbumin (α-phytalbumose) and abrusglobin. The seed also contains an enzyme, abric acid and a coloring principle.

The roots are known as **Wild or Indian Liquorice** and contain 1.5 per cent of a substance resembling glycyrrhizin. They also contain 8 per cent of an acrid resin and a small quantity of an alkaloid, abrine, which precludes the root being substituted for glycyrrhiza. The leaves yield about 10 per cent of glycyrrhizin. Owing to their toxic properties, care should be exercised if the seeds are used by children. Abrus is an irritant to mucous membranes, occasionally used by ophthalmologists. It is a poison.

Robinia or Locust Bark is the bark of *Robinia pseudacacia*, the common locust tree. It possesses highly poisonous properties due to the presence of a protein, robin, which is soluble in water.

Jamaica Dogwood is the root bark of *Piscidia erythrina*, a tree growing in the West Indies. The bark has long been used for stupefying fish. It contains piscidin and piscidic acid and has been employed in medicine as a narcotic, analgesic and soporific.

Loco-Weed (*Astragalus crotalaria*), growing in California, Nebraska and Texas, is poisonous to cattle, horses, etc., causing a spinal tetanic reaction.

Scarlet Runner Bean, the fruit or seed of *Phaseolus multiflorus*, is largely used as a food, both in the form of "string" beans and dry beans. *Phaseolus* is the ancient classical name for the bean; *multiflorus* means many-flowered. It has been stated that the roots of this plant are narcotic and poisonous.

Erythrophlœum or Sassy Bark is the bark of *Erythrophlœum guineense*, a tree indigenous to central and western Africa. It has been employed by the natives of western Africa as an ordeal in their trials for witchcraft and sorcery, as well as for other criminal purposes, and apparently also enters into the composition of the arrow-poison of the Pigmies. A chemical examination of the bark resulted in the isolation of a highly toxic alkaloid, erythrophleine. Neither this alkaloid nor its salts could, however, be obtained in a crystalline state.

GERANIACEÆ, OR GERANIUM FAMILY

This is a small family of about 500 species, native to temperate climates and most abundant in South Africa. The flowers are perfect, regular 5-merous and hypogynous. The fruit is an elastically dehiscent capsule, separating with its long styles from the axis.

Geranium, or Cranesbill (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the dried rhizome of *Geranium maculatum*, a perennial herb indigenous to Canada and the eastern and central United States. The rhizome is collected in late summer or early autumn and is horizontal, cylindrical, tuberculate, or irregularly curved, 2.5 to 10 cm. in length, 3 to 15 mm. in diameter; externally it is dark brown, wrinkled, the upper and side portions with numerous buds or circular stem-scars, the under surface with numerous root-scars; the fracture is short; internally it is light brown, with thin bark, indistinct wood and large pith. The odor is slight and the taste astringent.

Geranium contains from 15 to 25 per cent of a gallitannin and is employed as an astringent.

LINACEÆ, OR FLAX FAMILY

A small family of herbs and shrubs comprising about 9 genera and 150 species, having perfect, regular, 4- to 6-merous, hypogynous and nearly symmetrical flowers. The fruit is usually a capsule, containing 1 to 2 seeds in each locule, there usually being twice as many locules as there are styles. Of special anatomical interest is the mucilaginous epidermal layer in the seeds and leaves of *Linum*. Calcium oxalate is secreted only in the form of solitary crystals. The non-glandular hairs are of the unicellular type. Glandular hairs, when present, always have a multicellular stalk. The tracheæ usually have simple pores and the sclerenchymatous fibers are generally marked by bordered pores.

LINSEED

Linseed, or Flaxseed (U. S. P. 1920 to 1947; N. F. 1947 to date) is the dried ripe seed of *Linum usitatissimum* Linné. The generic name *Linum* is from the Latin *linea*, meaning thread, and refers to the use of the flax fibers; *usitatissimum* is from the Latin and means "most useful." The plant is an annual which is cultivated in all temperate and tropical regions either for the fiber (flax) or for the seed. With the possible exception of cotton, perhaps no plant is of greater economic value or of wider geographical distribution. The useful products it yields may be tabulated as follows:

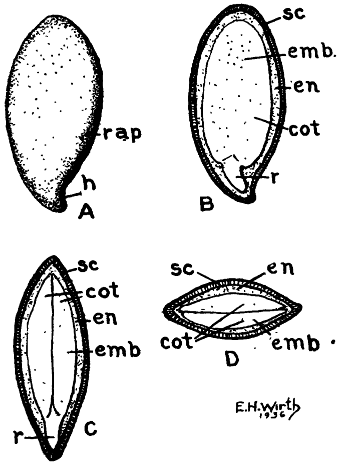
Flax Plant

- **Stem**
  - **Bast fibers** ↓ **Linen thread** ↓ lace, cloth, rugs, toweling, lawn and other fabrics
  - **Straw** ↓ pressed into sheets for building insulation, pulp for paper, etc.
- **Seed**
  - **Oil** ↓ paints, varnishes, linoleum, oilcloth, printers' ink, soaps, etc. (70,000,000 gals. produced in U. S. annually)
  - **Oil cake** ↓ cattle feed (about 600,000 tons produced in U. S. annually)

The annual crop is harvested when the fruits are fully mature, usually with the "combine" which separates and cleans the seed in the field. The oil is removed from the seed by expression.

The economic use of flax antedates all historical record. Seed and fabric made from the fibers of flax have been found in the remains of the Swiss Lake dwellings and the weaving of flax into cloth is illustrated on the Egyptian tombs. Mummy cloth dating back to at least 2300 B.C. is made from flax. The use of the seeds both as a food and medicine are mentioned by historians as early as the seventh century B.C. Charlemagne promoted the growth of flax in northern Europe.

Considerable flax is grown in North and South Dakota, Minnesota, Montana, Kansas, Southern California, Canada, Nebraska, Missouri, Wyoming, Wisconsin, Iowa in the United States and in many other countries. The U. S. production is about 30 million bushels of seed annually, and about 15 million bushels are imported from Canada, Europe and South America.



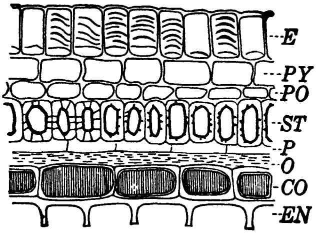


FIG. 186 FIG. 187

FIG. 186.—Linseed: *A*, whole seed; *B*, longitudinal section through the broad diameter of the seed; *C*, longitudinal section through the narrow diameter of the seed; *D*, transverse section through the seed; *h*, hilum; *rap*, raphé; *sc*, seed coats; *emb*, embryo; *en*, endosperm; *cot*, cotyledon; *r*, radicle. (Drawings by Wirth.)

FIG. 187.—Transverse section of Flaxseed: *E*, epidermal cells with small lumina and very thick outer wall showing mucilage lamellæ; *PY*, *PO*, parenchyma cells; *ST*, stone cells; *P*, parenchyma beneath stone cells; *O*, obliterated cells of the hyaline layer; *CO*, pigment cells with reddish brown contents; *EN*, endosperm.

DESCRIPTION AND STRUCTURE.—See Figures 186, 187, 188 and the National Formulary.

CONSTITUENTS.—Fixed oil, 30 to 40 per cent; proteins, about 25 per cent; mucilage; total ash, 4 per cent; acid-insoluble ash, 0.3 per cent.

STANDARDS.—Linseed contains not more than 2 per cent of other seeds or foreign organic matter, and yields not more than 6 per cent of ash, not less than 30 per cent of non-volatile, ether-soluble extractive, at least 98 per cent of which is saponifiable. It is practically free from starch; and upon defatting the powder and boiling it with 50 parts of water, the filtered solution does not show more than a faint blue color upon the addition of iodine solution.

USES.—Linseed is a demulcent and an emollient. Flaxseed meal is employed as a poultice.

ALLIED PLANT.—In False Flax (*Camelina sativa*) of Europe the sclerenchymatous fibers are replaced by broad, short stone cells, and the epidermal cells on the addition of water eject a central column of mucilage.

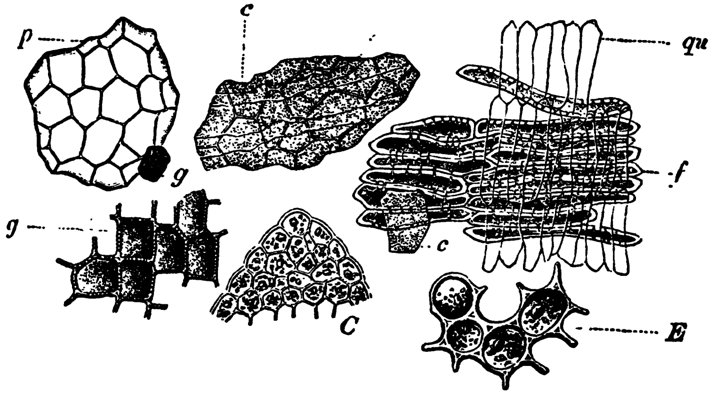


FIG. 188.—Linseed or Flaxseed Meal: yellow with numerous brown fragments; *P*, epidermis with mucilaginous epidermal cells; *c*, epidermal cells with broken cutinized layer; *E*, subepidermal cells of a yellowish color; *f*, sclerenchymatous fibers, 100 to 250 microns in length, about 10 microns in diameter, and with numerous simple pores; *qu*, colorless, more or less obliterated "cross-cells"; *g*, pigment cells, some tabular, polygonal or tangentially elongated, and with a reddish or yellowish brown pigment which is colored dark blue with solutions of ferric chloride; *c*, cells of endosperm and embryo containing oil and aleurone grains; the crystalloids of the aleurone grains can be readily discerned on treating the material first with chloroform and then mounting in an iodine solution. (After Moeller.)

Linseed Oil, Flaxseed Oil, or Raw Linseed Oil (U. S. P. 1820 to 1947; N. F. 1947 to date) is the fixed oil obtained from linseed. In the preparation of linseed oil the seeds are first crushed to break the seed coats. The crushed seeds are then subjected to hydraulic pressure, usually accompanied by heat and the oil removed by expression.

DESCRIPTION.—A yellow oily liquid having a peculiar odor and a disagreeable taste. When exposed to the air, it gradually thickens, darkens in color, and acquires a more pronounced odor and taste.

CONSTITUENTS.—Linseed oil contains glycerides of the following unsaturated fatty acids: linolic (about 15 per cent), linolenic (about 15 per cent) and isolinolenic (about 65 per cent). It also contains glycerides of the following saturated acids: myristic, stearic and palmitic.

STANDARDS.—For use in paint, linseed oil is boiled with driers, such as litharge, which form metallic salts. These salts hasten the drying of the oil. Linseed oil that has been "boiled" or treated with a drier must not be used medicinally. Linseed oil must be free from non-drying oils, mineral or rosin oils, and rosin; the free fatty acids in 10 gm. must be not more than the equivalent of 7.5 cc. of tenth-normal sodium hydroxide; the unsaponifiable matter must be not more than 1.5 per cent; the saponification value not less than 187 and not more than 195, and the iodine value not less than 170.

Uses.—Linseed Oil is a demulcent and a laxative when taken internally. It is applied externally, usually in the form of **Linimentum Calcis** or **Carron Oil** (U. S. P. 1820 to 1936; N. F. 1936 to date), for burns, scalds, etc.

Flaxseed Meal or Linseed Meal (U. S. P. 1863 to 1882) is usually mentioned in the official monograph, though a separate monograph for it is no longer included in the Pharmacopœia. It is commonly prepared from the linseed "oil-cake" remaining after the expression of most of the oil, though up to 10 per cent of the weight of the oil-cake can be extracted by volatile solvents. It is used very extensively as a laxative in stock feed mixtures.

Flaxseed meal sometimes contains small quantities of rye or wheat grains, unintentionally mixed with the flaxseed or because the meal was shipped in second-hand flour sacks. To prevent infestation with maggots keep flaxseed meal in well-closed containers containing a small amount of carbon tetrachloride.

ERYTHROXYLACEÆ, OR COCA FAMILY

This is a very small family, represented by 2 genera, the more important of which is *Erythroxylon*. They are mostly tropical shrubs with entire leaves and 5-merous flowers, and the fruit is a 1-seeded, reddish drupe resembling that of dogwood. The anatomy of the plants of this family closely resembles that of the *Linaceæ*. Of especial interest is the development of papillæ on the dorsal surface of the leaves. This is found in most species of *Erythroxylon*.

COCA

Coca or Coca Leaves (U. S. P. 1882 to 1916) is the dried leaves of *Erythroxylon Coca* Lamarck, known commercially as Huanuco Coca (U. S. P. 1882 to 1916), or of *Erythroxylon truxillense* Rusby, known commercially as Truxillo Coca (U. S. P. 1905 to 1916), or of *E. novogranàtense* (Morris) Hieron, known commercially as Peruvian Coca (never official).

The plants are shrubs or small trees attaining the height of about 2 meters, indigenous to Peru (*E. truxillense*) and Bolivia (*E. coca*), and cultivated not only in these countries but also in Java (*E. truxillense*), and to some extent in Ceylon. *Erythroxylon* is from two Greek words meaning red and wood, alluding to the color of the plants; *coca* is the Spanish name for the tree; and *truxillense* is from Truxillo, a coast city in northern Peru.

Most of the present day supply of the drug is obtained from cultivated plants grown at an altitude of 1500 to 6000 feet in Peru and Bolivia. The leaves are collected from the twigs cut off in the spring pruning, again in June and the third time in the fall. Only a very small portion of the drug is exported, most of it being chewed by the natives or used for the manufacture of cocaine. Peru exports a considerable quantity of crude cocaine.

Coca leaves were highly valued by the natives long before the Spanish conquest, the tree being known as "The Divine Plant of the Incas." Monardes published an extensive article on the drug in 1569. The natives chew the leaf, either as such or mixed with lime, and are thus able to travel great distances, often with heavy loads, without experiencing fatigue and without any but the most meager food rations. Cocaine was first isolated in 1860, but until 1884, coca was considered as but an inferior substitute for tea. In that year Koller discovered its local anesthetic properties.

Huanuco Coca Leaves are oval, obovate or elliptical, 3 to 7 cm. in length 2 to 3 cm. in breadth (Fig. 189), with an acute, slightly mucronate apex, an acute base, and an entire, somewhat revolute margin. The upper surface is dark green, glabrous, and the under surface yellowish green and distinctly undulate with numerous minute papillæ. A parallel line about 4 mm. from the midrib on either side and extending from the base to the summit is often noted.

The texture is somewhat coriaceous, the odor distinct, and the taste bitter, producing a sensation of numbness.

Truxillo Coca Leaves are usually more broken, a little larger, and the curved line on either side of the midrib is usually wanting.

Javanese Coca Leaves resemble Truxillo coca and are employed for the manufacture of cocaine in Holland.

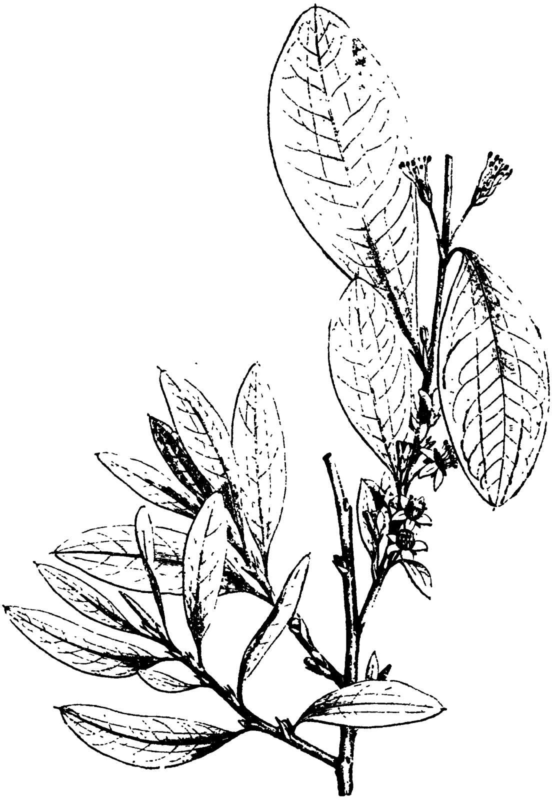


FIG. 189.—Flowering branch of *Erythroxylon coca*, showing the parallel lines on either side of the midrib, which are not true veins, but due to an extra development of hypodermal cells in this region. (After Reiche.)

Coca contains several alkaloids, including cocaine, cinnamyl-cocaine, α- and β-truxilline and ecgonine. Of these, cocaine is the most important, the Bolivian leaves containing the greatest amount, 0.5 to 1 per cent; the other alkaloids preponderate in the Peruvian leaves, which usually do not contain more than one-half or two-thirds as much cocaine as the Bolivian leaves; the Java leaves also contain benzoyl-pseudotropine; in addition, coca leaves contain a volatile aromatic principle; a tannin, giving a green color with solutions of ferric salts; and calcium oxalate. Young coca leaves contain more than twice as much total alkaloids as the older leaves.

Coca is used as a stimulant of the central nervous system in neurasthenia; it is habit-forming, and therefore dangerous to use. Its habitual use by the South American Indians disguises the sense of fatigue and hunger; long continued use undermines the health and produces an incurable insomnia, extreme emaciation, dropsy and death.

Cocaine (U. S. P. 1905 to date) is an alkaloid obtained from the leaves of *Erythroxylon Coca* Lamarck and other species of *Erythroxylon*, or by synthesis from ecgonine or its derivatives.

Cocaine Hydrochloride (U. S. P. 1894 to date) is the hydrochloride of the alkaloid cocaine.

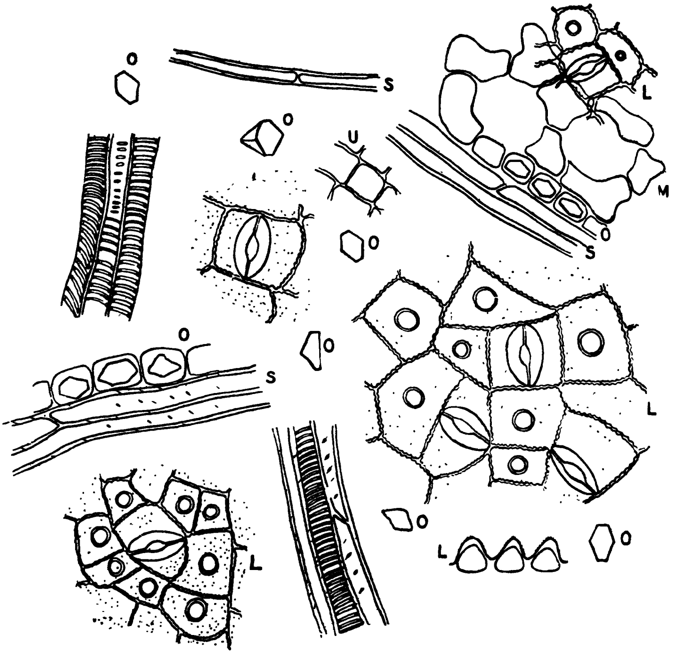
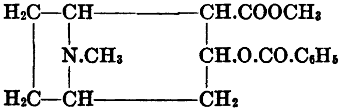


FIG. 190.—Powdered Coca: dark green fragments; the lower epidermis (*L*) composed of more or less polygonal cells and elliptical stomata, the latter usually with two neighboring cells; papillæ of under surface appear as circular markings, one occurring in the center of each of the polygonal cells; calcium oxalate in monoclinic prisms (*O*) from 3 to 15 microns in diameter, occurring either singly or in crystal fibers; fragments of tracheæ and thin-walled sclerenchymatous fibers, (*S*); cells of the upper epidermis (*U*) and fragment of loose mesophyll parenchyma (*M*).

Cocaine is obtained by extracting the leaves with dilute acid, or by treating them with lime and extracting with an organic solvent. The alkaloids may be purified by transferring from one solvent to another and crystallization. Cocaine is the methyl ester of benzoyl-ecgonine:



$$\begin{array}{lll} H_2C\text{—} & CH\text{————} & CH.COOCH_3 \\ \vert & \vert & \vert \\ \vert & N.CH_3 & CH.O.CO.C_6H_5 \\ \vert & \vert & \vert \\ H_2C\text{—} & CH\text{————} & CH_2 \end{array}$$

When hydrolyzed it splits into ecgonine, benzoic acid and methyl alcohol. Cinnamyl-cocaine splits into ecgonine, methyl alcohol and cinnamic acid; while α- and β-truxilline split into ecgonine, methyl alcohol and α- and β-truxillic acids. (The truxillic acids are isomeric dicinnamic acids.) Very often the complete mixture of alkaloids is hydrolyzed, by boiling with hydrochloric acid and the ecgonine hydrochloride thus formed converted into the free base. The ecgonine is benzoylated and methylated, thus forming a larger yield of cocaine.

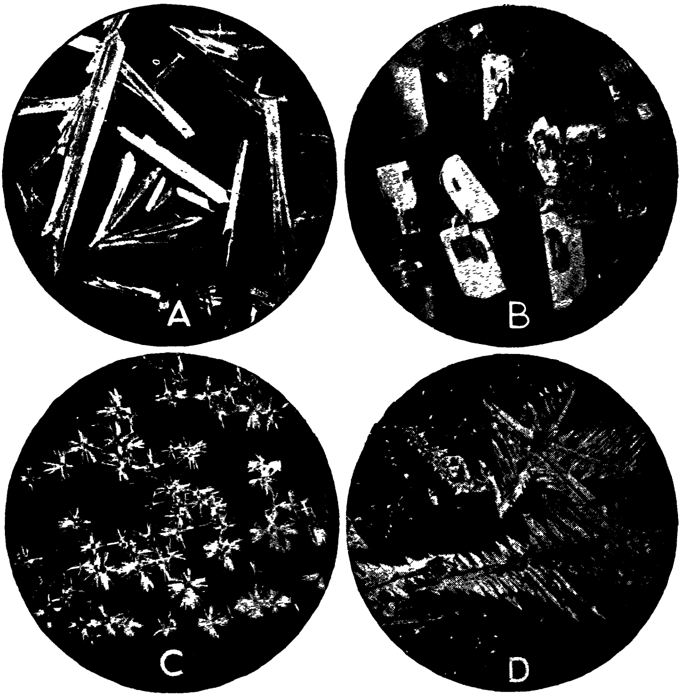


FIG. 191.—Cocaine: *A*, monoclinic crystals of cocaine; *B*, orthorhombic crystals of cocaine hydrochloride; *C*, monoclinic crystals of cocaine hydrochloride and palladous chloride; *D*, skeleton aggregates of cocaine hydrochloride and palladous chloride.

DESCRIPTION AND TESTS OF IDENTITY AND PURITY.—See Figures 191, 192, 193 and the U. S. Pharmacopœia.

USES AND DOSE.—Cocaine and cocaine hydrochloride are cerebral stimulants when taken internally, large doses, however, being narcotic. Externally they are local anesthetics. Average dose, 15 mg.

Synthetic Local Anesthetics have been produced, with a view of increasing stability and reducing toxicity and other injurious effects. Some of them are vasodilators and so are often employed in conjunction with epinephrine. They owe their origin to the discovery that the local anesthetic action of cocaine is due to the radicle of benzoic acid in combination with a nitrogen-containing basic group.

They may be classified into three general groups as follows:

COCAINE TYPE.—Readily soluble in water and effective either injected hypodermically or applied to the skin or to the mucous membrane.

Alypin Hydrochloride or Amydricaine Hydrochloride (NNR) is nearly as toxic as cocaine hydrochloride but is practically non-mydriatic, hence useful for optical application.

Amylcaine Hydrochloride (NNR) is like cocaine hydrochloride but non-mydriatic.

Butacaine Sulfate or Butyn Sulfate (NNR; U. S. P. 1942 to date) is somewhat more toxic than cocaine, but is useful for surface anesthesia.

Diothane Hydrochloride (NNR) is like cocaine but somewhat more toxic, three times as toxic as procaine.

Eucaine Hydrochloride or Betaeucaine Hydrochloride (U. S. P. 1916 to 1942; N. F. 1942 to date) is much less toxic than cocaine and is used extensively in the eye and on mucous surfaces.

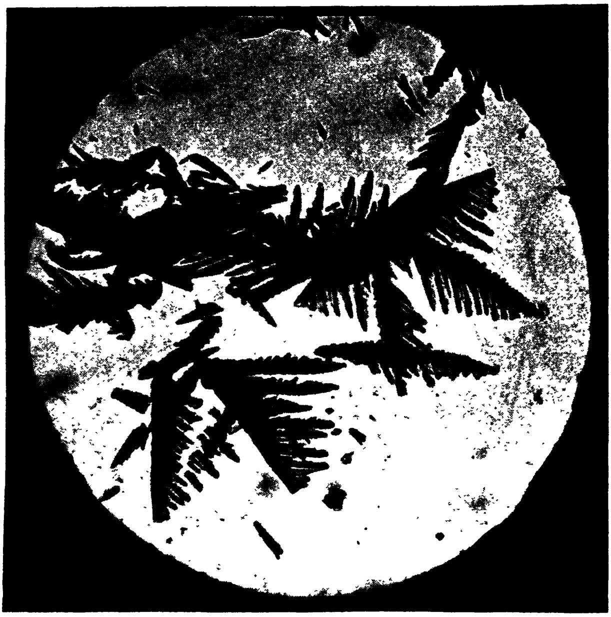


FIG. 192.—Crystals of cocaine chloro-platinate. To 0.5 cc. of a 1 per cent solution of cocaine are added 2 drops of platinum chloride test solution. The test-tube should not be shaken, as larger and better formed crystals will result when the solution is undisturbed. A buff-colored precipitate is formed which, under the microscope, appears as large feathers or plumes, sometimes arranged in stellate pattern. In higher dilutions (1:600) crystals slowly form which "resemble carpet tacks." Alpha-eucaine, with the above test, forms bundles of fine needles; beta-eucaine, after thirty minutes, gives a few large, leaf-like forms, rosettes and cubes; holocaine gives small stars; acoine gives an amorphous precipitate, while stovaine and euphthalmine give no precipitates. None of the precipitates yielded by the cocaine substitutes resemble the cocaine chloroplatinate in any way. (After Seiter and Enger.)

Phenacaine Hydrochloride or Holacaine Hydrochloride (NNR; U. S. P. 1936 to date) is more rapid in action, especially in the eye, than cocaine.

Tutocaine Hydrochloride or Butamin (NNR) is used for surface anesthesia in low concentration, giving a complete and prolonged effect.

PROCAINE TYPE.—Readily soluble in water, very effective, but anesthetic effect much less sustained than that of cocaine. Because of a tendency to dilate the blood-vessels, epinephrine is frequently used with the anesthetic in the hypodermic injection. Relatively ineffective for surface anesthesia.

Apothesine Hydrochloride (NNR) is slower in action and more toxic than procaine, but less toxic than cocaine.

Larocaine Hydrochloride (NNR) is like procaine, useful in surface and infiltration anesthesia, quick in action and of long duration.

Metycaine Hydrochloride (NNR) is useful in surface anesthesia; subcutaneously it is three times as toxic as procaine.

Nupercaine Hydrochloride or Dibucaine Hydrochloride (NNR) is very powerful and toxic; used in doses about one-tenth of those of procaine hydrochloride.

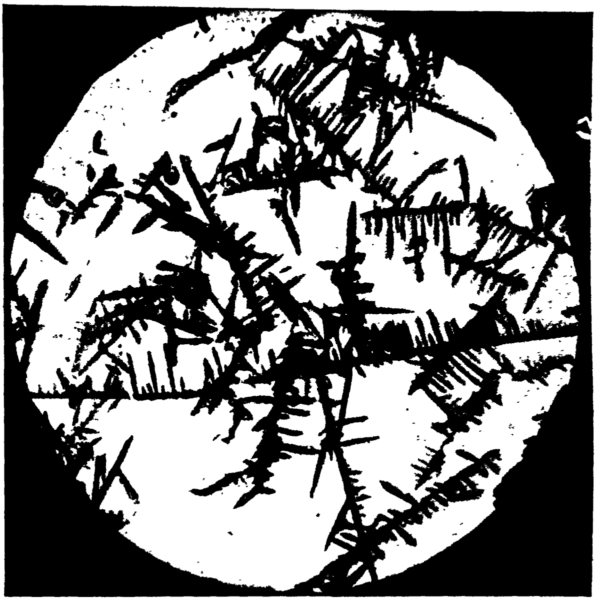


FIG. 193.—Crystals of cocaine-chloro-aurate. To 1 cc. of a dilute solution (1:300) of cocaine are added 3 drops of gold chloride test solution, avoiding shaking as in the case of the platinum chloride test. A precipitate immediately forms and slowly changes from the amorphous into the crystalline state. Under the microscope, the crystals resemble fern-fronds, generally with a stellate arrangement. In dilutions of 1:12,000, similar crystals form after long standing. With the gold test, alpha-eucaine gives branching, twig-like crystals; stovaine gives large crystals resembling those of cocaine chloroplatinate in general structure, but differing in that the branches possess smaller branches which is not the case with the cocaine chloroplatinate. Amorphous precipitates are given with beta-eucaine, acoine and holocaine. Euphthalmine gives no precipitate. (After Seiter and Enger.)

Procaine Hydrochloride or Novocaine Hydrochloride (NNR; U. S. P. 1926 to date) is less toxic than cocaine and the effect is less sustained.

Procaine Borate (NNR).
Procaine Nitrate (NNR).

Tetracaine Hydrochloride, Pontocaine Hydrochloride or Amethocaine Hydrochloride (NNR; U. S. P. 1942 to date) is like procaine in action but effective in somewhat lower concentration.

ANESTHESIN TYPE.—Slightly soluble in water, hence but slightly effective or irritant or toxic, hypodermically or internally, and seldom so used. Effective in wounds, ulcers, and on the mucus membrane in the form of dusting powder, ointment or suppositories.

Butyl Aminobenzoate or Butesin (NNR; U. S. P. 1942 to date).

Butesin Picrate (NNR).

Ethyl Aminobenzoate, Anesthesin or Benzocaine (NNR; U. S. P. 1926 to date).

Orthoform-New (NNR) is used mostly externally in wounds.

ZYGOPHYLLACEÆ, OR CALTROP FAMILY

The plants are mostly herbs and shrubs which are widely distributed in warm-tropical regions. The leaves are mostly opposite, pinnate and stipulate. The flowers are perfect, regular and mostly 5-merous. The fruit is usually capsular. The hairs are usually simple and unicellular; occasionally there is a metamorphosis of the wall to form a resinous excretion. True glandular hairs do not occur in the plants of this family. Mucilage cells and tannin-secreting cells are occasionally present. The tracheæ usually have simple pores and in *Guajacum* are filled with resin. Calcium oxalate is secreted in the leaves in the form of rosette aggregates and in the axis in solitary crystals.

GUAIAC

Guaiac Wood or Lignum Vitæ (U. S. P. 1820 to 1905; N. F. 1916 to 1926) is the heartwood of *Guajacum officinale* Linné, or of *Guajacum sanctum* Linné. The name *Guajacum* is from the Spanish *guayaco,* the native Haitian name of the plant; *officinale* means used or found in the workshop of the pharmacist; *sanctum* means holy, sacred or consecrated. The plants are small evergreen trees, *G. officinale* being found in Colombia, Venezuela and in the West Indies, while *G. sanctum* is found in Cuba, Haiti and the Bahamas.

Guaiac wood is extremely hard and is used in the manufacture of mallets and other wooden articles where hardness is a requisite. As a drug, it usually appears in the form of dark brown or greenish brown chips which contain about 15 per cent of resin and also saponins. Its medicinal use is similar to that of the resin.

Guaiac or Guaiac Resin (U. S. P. 1820 to 1926; N. F. 1926 to date) is the resin obtained from guaiac wood by boiling the chips with water, the melted resin rising to the top; it is then removed from the water, strained and dried. Formerly, a log was bored longitudinally and heated in a sloping position, the resin melting and flowing from the end of the log. Guaiac was introduced into Europe from San Domingo in 1526 and became a popular remedy for syphilis.

Description.—Usually in irregular masses; externally greenish brown, frequently covered with a greenish powder; brittle, the fractured surface yellowish green or reddish brown with a glassy luster; more or less transparent in thin pieces; fusible; odor balsamic; taste somewhat acrid.

Guaiac melts between 85° and 90° C. It is readily soluble in alcohol, chloroform, ether and in solutions of the alkalis.

Constituents.—Guaiac contains several resin acids: a mixture of α- and β-guaiaconic acids, about 70 per cent; guaiaretic acid, 10 per cent; and guaiacinic acid, about 15 per cent.

Standards and Tests.—Guaiac yields not more than 15 per cent of alcohol-insoluble residue and not more than 2 per cent of acid-insoluble ash.

When 1 drop of ferric chloride T.S. is added to 5 cc. of a 1 per cent alcoholic solution of guaiac, a deep blue color forms which gradually changes to green and finally becomes yellow. When a mixture of 5 cc. of an alcoholic solution of guaiac and 5 cc. of water is shaken with 20 mg. of lead peroxide, a deep blue color is developed. If the solution is filtered and the filtrate boiled, the color is discharged, but may be regenerated by the subsequent addition of lead peroxide and shaking. The addition of hydrochloric acid also discharges the color. This blue color is due to the formation of "guaiac blue," an oxidation product of α-guaiaconic acid. It is formed by most oxidizing agents and an alcoholic solution of guaiac is employed as a test for the presence of oxydase enzymes. Guaiac should be free from adulteration with rosin, which may be detected by means of the cupric acetate test.

USES AND DOSE.—Guaiac is a stimulant, a diaphoretic and an alterative. Average dose, 1 gm.

Creosote Bush, Greasewood or *Larrea tridentata* is an evergreen shrub, 0.5 to 2 meters high and native to hot, arid regions in southwestern United States and adjacent Mexico. The plant is profusely-branching, with numerous small olive green leaves, and small yellow flowers in early spring. The leaves and stipules are covered with an exudate, having a creosote odor, and containing 17 per cent (of the weight of the leaves) of resin, 12 per cent of mucilage, a volatile oil and cresols or phenols. The exudate is produced by metamorphosis of the walls of the epidermis and trichomes. The separated exudate is known as Sonora Gum. An infusion of the leaves has been used in throat, bronchial and pulmonary complaints.

RUTACEÆ, OR RUE FAMILY

Most of the members of this family, which numbers about 120 genera and 900 species, are trees and shrubs, with compound leaves, regular, 3- to 5-merous flowers and capsular fruits. With very few exceptions they possess schizogenous or schizolysigenous cavities in the branches and leaves, giving rise to transparent dots in the latter. They usually have isolated groups of bast fibers in the pericycle; in *Pilocarpus,* however, there is a composite and continuous sclerenchymatous ring. Calcium oxalate is usually secreted in the form of rosette aggregates, but styloids, raphides and membrane crystals are also present, the latter being especially prominent in the genus *Citrus.* Both glandular and non-glandular hairs are present, stellate hairs being quite common in the family.

ORANGE

Sweet Orange Peel (U. S. P. 1820 to date) is the fresh, outer rind of the non-artificially colored ripe fruit of *Citrus sinensis* Linné. The inner, white portion of the rind should be excluded. *Citrus* is the ancient Latin name for the plant; *aurantium* refers to the golden yellow color of the fruit; *sinensis* indicates that the plant is cultivated in China. The plant is a tree of medium height and appears to have originally come from China, although at present it is cultivated in many subtropical localities, our supply coming largely from California and Florida. The pulp of the **sweet orange** is eaten as a delicacy and the juice consumed as a beverage. Both the pulp and juice are rich in vitamin C, and contain citric and other fruit acids and sugars. The sweet orange was not known to the ancient Greeks and Romans and was first brought from China by the Portuguese in the fifteenth century. It was cultivated in Southern Europe and later in Florida and California.

Description.—The outer, orange yellow layer recently separated by grating or paring and consisting of epidermal cells, thick-walled parenchyma cells of the sarcocarp, with chromoplastids and occasionally calcium oxalate in monoclinic prisms 0.020 to 0.035 mm. in length, schizolysigenous oil cavities and globules of volatile oil; odor highly fragrant; taste pungently aromatic.

Constituents.—Volatile oil; bitter principles are practically absent.

Uses.—Sweet orange peel is an aromatic; it is used for flavoring other medicines.

Orange Oil or Oil of Sweet Orange (U. S. P. 1882 to date) is the volatile oil obtained by expression from the fresh peel of the ripe fruit of *Citrus sinensis* Linné. The usual methods for obtaining the oil are described under oil of lemon (page 375).

Description and Tests.—See the U. S. Pharmacopœia.

Constituents.—Oil of orange contains about 90 per cent of the terpene *d*-limonene, about 5 per cent of citral, citronellal and the methyl ester of anthranylic acid.

Standards.—Oil of orange which has a terebinthinate odor must not be used or dispensed. This odor is usually caused by the partial decomposition of the limonene which takes place upon exposure of the oil to air and light.

Uses and Dose.—Oil of orange is principally used as a flavoring agent, although it is slightly carminative. Average dose, 0.1 cc.

Bitter Orange Peel (U. S. P. 1831 to date) is the dried rind of the unripe fruit of *Citrus Aurantium* Linné. The plant is a tree resembling the sweet orange tree, the latter being a variety of the former. Although a native of India it is widely cultivated in subtropical localities. The peel is removed from the unripe fruit by quartering or peeling spirally. The commercial article is obtained from Spain, Sicily, Tripoli and warm temperate South America. The bitter orange tree seems to have been introduced into Arabia, Africa and Syria by the Arabs, and subsequently reached Europe about 1200 A.D.

Description.—In quarters or irregular ribbons 2 to 6 mm. in thickness; outer surface weak brown to moderate olive with a green tinge, numerous small pits and fine reticulate ridges; inner surface, yellowish with many slight conical projections; fracture hard, short.

Structure.—See Figure 194.

Powder.—Weak yellow to weak greenish yellow; odor fragrant and aromatic; taste aromatic and bitter; parenchyma walls from 4 to 12 microns thick, tracheæ very small with close spiral markings or simple pores; calcium oxalate prisms from 15 to 45 microns long.

Constituents.—Volatile oil, resembling that of sweet orange peel but with a superior flavor and a bitter taste; several bitter principles: (*a*) aurantiamarin (1.5 to 2.5 per cent), an amorphous, bitter glucoside, to which the bitter taste is chiefly due; (*b*) aurantiamaric acid (0.1 per cent), a very bitter, green amorphous, resinous principle; (*c*) naringin (aurantin), a yellowish, crystalline, bitter glucoside; (*d*) isohesperidin (0.4 to 3 per cent), a slightly bitter glucoside; a fixed oil; a resin; a principle resembling tannin; and **Hesperidin,** a tasteless glucoside, 5 to 8 per cent. It forms white sphere-crystals on placing the fresh fruit in alcohol. It is colored reddish brown with solutions of ferric chloride, and on hydrolysis yields 1 molecule of rhamnose, 2 of glucose and 1 of hesperetin, a sweet principle which crystallizes in prisms. Total ash, about 4.3 per cent; acid-insoluble ash, 0.07 per cent.

Uses.—Bitter orange peel is a tonic and a stomachic. It is also a carminative and stimulant.

Orange Berries are the immature fruits of *Citrus Aurantium* Linné. They are nearly globular, 5 to 20 mm. in diameter, greenish or brownish black, granular rugose; the internal structure resembles that of orange fruits, but the seeds are rudimentary and the taste is aromatic and bitter. They are used for the same purposes as bitter orange peel.

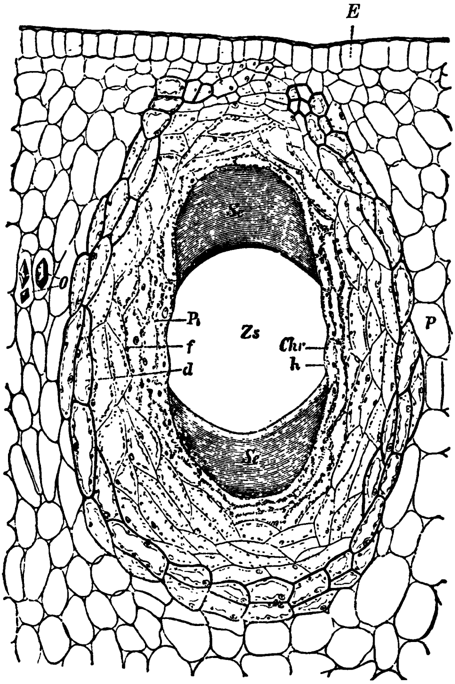


Fig. 194.—*Citrus vulgaris.* Longitudinal section of a young fresh fruit showing a lysigenous oil canal or duct: *Se*, oil; *Zs*, cell sap; *Pi*, cells in which the walls have been dissolved; *f*, thinwalled cells; *d*, thick-walled cells; *k*, nucleus; *Chr*, chromoplasts; *o*, crystals of calcium oxalate; *E*, epidermis. (After Meyer.)

Bitter Orange Oil (N. F. 1916 to date) is a volatile oil obtained by expression from the fresh peel of the fruit of *Citrus Aurantium* Linné. The oil is obtained by one of the methods described under oil of lemon. It is similar to oil of sweet orange, but is generally conceded to be superior to it in flavor. Consult the National Formulary for its characteristics.

Uses and Dose.—Bitter orange oil is a flavor, a stimulant and a carminative. Average dose, 0.1 cc.

Orange Flowers (U. S. P. 1863 to 1894) consists of the dried unexpanded flowers of *Citrus Aurantium* Linné (var. *vulgaris* or *Bigarade* or *amara*). The bitter orange orchards of southern France, Italy, Sicily and Argentina are largely for the purpose of preparing oil of orange flowers by distillation. The fresh flowers yield from 0.6 to 1 per cent of the oil.

The dried flowers are rather cylindrical, up to 25 mm. in length and 8 mm. in diameter, yellowish or light tan in color, though before drying the fleshy petals are intensely white; odor fragrant, though less so than the fresh flowers.

The dried flowers were used for the preparation of orange flower water before the French or Sicilian product was preserved and imported into this country.

Orange Flower Oil or Oil of Neroli (U. S. P. 1882 to 1905; N. F. 1916 to date) is the volatile oil distilled from the fresh flowers of *Citrus Aurantium* Linné. The aqueous distillate after removal of the oil constitutes **Orange Flower Water** (U. S. P. 1863 to date).

Consult the National Formulary for description, constants and tests.

The oil consists of a complex mixture of the terpenes, *l*-pinene, *l*-camphene, dipentene, limonene, and about 47 per cent of terpene alcohols and their acetates, such as *l*-linalool, *d*-terpineol, geraniol, and nerol.

The oil and the orange flower water are used as pleasant flavorings in some pharmaceutical preparations; also to a considerable extent in the perfume and cosmetic industries.

LEMON

Lemon (U. S. P. 1820 to 1863) is the fruit of *Citrus Limon* (Linné) Burmann filius.

Lemon Peel (U. S. P. 1842 to date) is the outer yellow rind of the fresh ripe fruit of *Citrus Limon* (Linné) Burmann filius. *Limon* is from *limun,* the name of the fruit. The plant is a small evergreen tree with shining leaves, indigenous to northern India but cultivated to a considerable extent in subtropical regions, among which the following might be mentioned: southern Spain, southern Italy, Sicily, southern California, Florida, Jamaica and Australia. The history of the lemon parallels that of the orange; it has been known from the beginning of the written history of India, its native land. It was brought to the levant by the Arabs and either by them or by the Crusaders introduced into Europe during the twelfth century.

DESCRIPTION.—The outer, lemon-yellow or dark yellow layer is removed by grating or paring. It is of a highly fragrant, distinctive odor and aromatic taste.

STRUCTURE.—An epidermal layer composed of small tabular cells, a hypodermal layer containing numerous yellow chromoplastids, a mesocarp with colorless, thin-walled parenchyma and large, ellipsoidal schizolysigenous oil cavities; parenchyma cells contain a layer of granular protoplasm adhering to the walls and occasionally membrane crystals of calcium oxalate, which are irregularly polygonal in shape, polarize light strongly and are from 15 to 25 microns in diameter.

CONSTITUENTS.—Volatile oil; a very small quantity of hesperidin; bitter principles; a principle resembling tannin; calcium oxalate. Total ash, about 4 per cent; acid-insoluble ash, about 0.1 per cent.

USES.—Lemon peel is a flavoring agent, a stimulant and a stomachic. It is employed chiefly in combination with other drugs.

Lemon Juice (U. S. P. 1863 to 1916) contains 5 to 8 per cent of citric acid, in part free and also combined as an ester; saccharose, 0.52 per cent; invert sugar, 1.42 per cent; extractive, 10.44 per cent; nitrogenous substances, 0.32 per cent; and ash, 0.2 per cent, the latter consisting chiefly of potassium and calcium phosphates.

Besides the above-mentioned constituents which make it valuable as a refrigerant drink, lemon juice is also high in vitamin C content.

Citric Acid (U. S. P. 1820 to date) was first isolated from lemon juice by Scheele in crystal form in 1784. It is present in many fruits and plants, and commercially is obtained from lemons, limes or pineapples, but mostly by fermentation of sucrose. It occurs in colorless, odorless, translucent crystals and is readily soluble in water and alcohol. It is used in refrigerant and diuretic beverages. Industrially it serves a wide variety of uses.

Lemon Oil (U. S. P. 1820 to date) is the volatile oil obtained by expression, without the aid of heat, from the fresh peel of the fruit of *Citrus Limon* Linné, with or without the previous separation of the pulp and the peel. There are six processes utilized in the recovery of oil of lemon, four of which yield an oil meeting the pharmacopœial requirements. (1) The outer portion of the rind which contains the volatile oil is removed by grating and the resulting raspings placed in canvas bags and subjected to pressure. The resulting turbid oil is allowed to stand until the sediment separates, after which the oil is decanted. (2) The sponge process is employed to a considerable extent in Sicily and along the Riviera. The lemon is peeled and pieces of the peel are pressed flat so as to flex them and rupture the oil cells. The oil is absorbed by the sponge which, when it becomes saturated, is squeezed out, and the process repeated. (3) The entire fruits are rotated in a saucer-shaped container having several rows of sharp metal pins and called an *écuellé a piquer.* The pins rupture the oil cells, the exuding oil collecting in a long narrow depression in the bottom of the saucer, which also serves as the handle. (4) In the machine process used in Italy the oil is separated mechanically, the principle of which simulates that of the *écuellé a piquer.* (5) Cold-pressed California oil is obtained by the application of extremely high pressure to the lemons and the very rapid removal of the juice and oil, which mixture is then separated by high-speed centrifugal separation at the lowest feasible temperature and in the shortest possible time. (6) Some oil of lemon is obtained by distillation. Such oil is not comparable with the expressed oil and does not conform to the pharmacopœial definition. Distilled oil is usually used for the preparation of terpeneless oil of lemon.

DESCRIPTION, CONSTANTS AND TESTS.—See the U. S. Pharmacopœia.

CONSTITUENTS.—Oil of lemon contains about 90 per cent of terpenes consisting chiefly of *d*-limonene; about 4 per cent citral, which is the most important constituent, and small quantities of citronellal, geranyl acetate, terpineol, methyl heptenone, a sesquiterpene and octyl and nonyl aldehydes.

STANDARDS.—Oil of lemon which has a terebinthinate odor must not be used or dispensed (decomposed terpenes or added oil of turpentine).

USES AND DOSE.—Oil of lemon is a stimulant, carminative and stomachic. It is largely used as a flavor. Average dose, 0.1 cc.

ADULTERANTS.—Oil of turpentine was formerly used as an adulterant, but this has been replaced by terpenes obtained in the preparation of terpeneless oils. The U. S. P. X required the oil to contain at least 4 per cent citral, yet even such a citral content is no criterion of purity since citral from a cheaper source (oil of lemon grass which contains about 80 per cent citral) may be added. Only a careful check of the physical and chemical constants of the oil will determine its purity.

Terpeneless Oils.—Oil of lemon and oil of orange by virtue of their high terpene content often develop a terebinthinate odor on keeping. A considerable amount of these terpenes may be removed by distillation under reduced pressure.

A terpeneless oil of lemon with a citral content of 40 to 50 per cent may be prepared, and in terpeneless oil of orange about 95 per cent of the terpenes have been removed. Such oils have excellent keeping qualities and may be employed in smaller quantities to obtain the same organoleptic effect. They are, however, considerably higher in price than the natural oils.

PECTIN

Pectin (N. F. 1942 to date) is a purified carbohydrate product obtained from the dilute acid extract of the inner portion of the rind of citrus fruits or from apple pomace. It consists chiefly of partially methoxylated polygalacturonic acids. *Pectin* is from the Greek meaning congealed or curdled.

Pectin yields not less than 7 per cent of methoxyl groups and not less than 78 per cent of galacturonic acid. It differs from "commercial" pectin in that it contains no sugars or organic acids, but is pure pectin to which no additions have been made.

Pectin in fruit is in an insoluble form known as protopectin; it is converted to the soluble form by heating the fruit with dilute acid. This solution of pectin can be precipitated by means of alcohol or by "salting out;" then washed and dried.

Pectin occurs as a coarse or fine powder, yellowish white in color, almost odorless and with a mucilaginous taste. It is completely soluble in 20 parts of water, the solution being viscous, opalescent, colloidal, and acid to litmus paper; one part of pectin heated in nine parts of water forms a stiff gel. For Tests of Identity and Purity see the National Formulary.

Pectin has a wide use as a gel in pharmacy, as well as in cookery and commercially. Therapeutically, the preserved pectin paste is valuable in the healing of ulcers, acting to keep out air and infection from the decaying flesh; possibly it stimulates the growth of new cells.

BERGAMOT OIL

Bergamot Oil (U. S. P. 1842 to 1905; N. F. 1916 to date) is a volatile oil obtained by expression from the rind of the fresh fruit of *Citrus Bergamia* Risso et Poiteau. The name *bergamia* is from the Turkish *beg-armudi*, meaning literally *prince's pear* and refers to the pear-shaped fruit. The plant is a small tree yielding non-edible fruits having a thick yellow rind from which the volatile oil is obtained by expression. The trees are cultivated in southern Europe, Asia and tropical America, Italy and France yielding most of the commercial supply.

CONSTITUENTS.—Oil of bergamot yields not less than 36 per cent of esters, calculated as linalyl acetate $C_{10}H_{17}C_2H_3O$.

USES.—Oil of bergamot is used as a perfume, being especially adapted for hair tonics and other external preparations.

Lime Juice (N. F. 1916 to 1926) is the juice expressed from the fresh fruit of *Citrus aurantifolia*. It contains from 5 to 10 per cent of citric acid and is used in refrigerant drinks.

Citron is the fruit of *Citrus Medica* Linné. The fruit is large and the thick rind is "candied" to form a popular confection.

Grapefruit is the ripe fruit of *Citrus paradisi*, and is widely used as a succulent and refrigerant food, rich in vitamin C.

Bael Fruit or Bengal Quince is the fruit of *Ægle marmelos*, a tree indigenous to India. The fruit somewhat resembles an orange; its mucilaginous pulp is mildly astringent, although it contains no tannin. It has been used in diarrhea and dysentery.

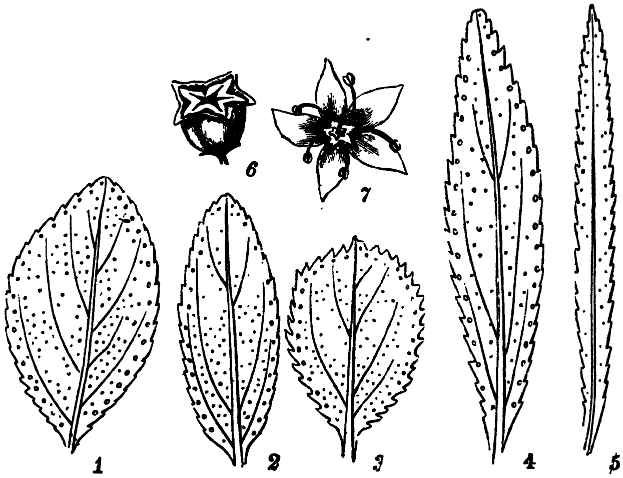


FIG. 195.—Buchu leaves, showing oil cavities which give the leaves a glandular-punctuate appearance: 1, *Barosma crenata ovalis;* 2, *B. crenulata latifolia;* 3, *B. betulina;* 4, *B. serratifolia;* 5, *Empleurum ensatum;* 6, dehiscent fruit of *B. crenulata;* 7, flower of the same. (After Tschirch.)

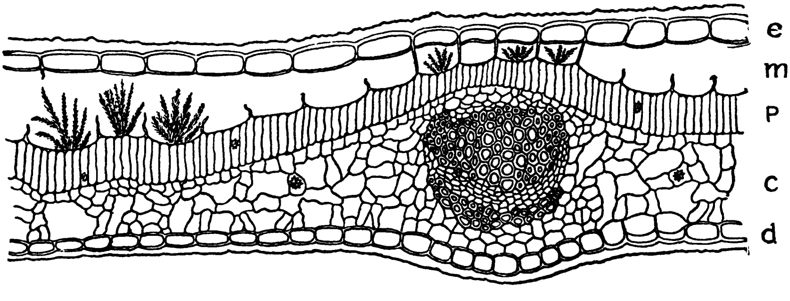


FIG. 196.—Transverse section through the leaf of *Barosma serratifolia* Willd: *e*, epidermal cells of upper surface, the inner walls of which are mucilaginous and resting upon a single row of hypodermal cells mostly mucilaginized. The mucilage (*m*) frequently includes dendritic excretions of diosmin in the form of feather-like aggregates, which dissolve in solutions of potassium hydroxide, giving a yellow color; *p*, palisade cells, some of which contain rosette aggregates of calcium oxalate; *c*, chlorenchyma, some of the cells containing rosette aggregates of calcium oxalate, also a large vascular bundle (mestome strand) with a steromatic pericycle forming an arch on the dorsal face; *d*, epidermis of lower (or dorsal) face of the leaf. (After Solereder.)

BUCHU

Buchu (U. S. P. 1842 to 1936; N. F. 1936 to date) is the dried leaf of *Barosma betulina* (Thunberg) Bartling et Wendland, known in commerce as Short Buchu (1842 to date); or of *Barosma crenulata* (Linné) Hooker, known in commerce as Oval Buchu (1842 to 1905, 1926 to date, though sometimes called Short Buchu); or of *Barosma serratifolia*

(Curtis) Willdenow, known in commerce as Long Buchu (1882 to 1894, 1916 to date).

Buchu is from the Zulu name for the drug, *bucu; Barosma* refers to the heavy odor of the leaves; *serratifolia* and *crenulata* refer to the character of the margins of the leaves; and *betulina* means birch-leaf-like.

The plants are low shrubs indigenous to Cape Colony, S. Africa, and the drug is collected from the wild plants. Buchu was in use by the Hottentots when white men first visited this territory, and was introduced into Europe about 1821 by the Cape Colony colonists.

DESCRIPTION AND STRUCTURE.—See Figures 195 and 196 and the National Formulary.

POWDER.—Greenish yellow; odor aromatic, mint-like; taste camphoraceous; calcium oxalate in rosettes, 15 to 30 microns in diameter; epidermal cells with irregular masses or sphere crystals of diosmin, 30 to 500 microns in diameter, and with walls modified to mucilage; few simple hairs; fragments of lower epidermal tissue with numerous stomata; fragments of chlorenchyma with numerous oil-secretion cavities and oil globules.

CONSTITUENTS.—Short buchu contains from 1.2 to 1.45 per cent of a volatile oil, and long buchu contains about one-third as much; the oil contains about 30 per cent of diosphenol or buchu camphor, a phenolic ketone melting at 82° and boiling at 232° C.; the terpines *d*-limonene and dipentene; and the ketone *l*-menthone. Buchu also contains the glucoside diosmin which resembles hesperidin. (Diosmin has been reported as hesperidin in many plants.) It yields glucose, rhamnose and diosmetine on hydrolysis.

STANDARDS.—Buchu contains not more than 8 per cent of the stems of the plants yielding buchu and not more than 2 per cent of other foreign organic matter, and yields not more than 1 per cent of acid-insoluble ash.

USES AND DOSE.—Buchu is a diuretic and a carminative. The volatile oil is excreted by the kidneys, rendering the urine slightly antiseptic. Average dose, 2 gm.

ADULTERANTS AND SUBSTITUTES.—The leaves of *Empleurum ensatum* (see Fig. 195) have been offered for long buchu. They have a bitter taste and yield about 1 per cent of a volatile oil which does not contain a crystalline principle. The leaves of *Barosma venusta* resemble short buchu except for their much smaller size and the fact that an alcoholic extract gives a strong blue fluorescence in ultra-violet light. The trifoliate leaves of *Psoralea obliqua* are obtained from a South African shrub. The leaflets are oblique or unequal-sided, dentate, bitter and glandular and have numerous simple hairs.

Karoo Buchu is derived from *Diosma succulenta*, of South Africa. The leaves are ovate, 3 to 6 mm. in length, coriaceous, obtuse and slightly recurved at the apex. They yield an oil with a peppermint-like odor, containing diosphenol, and 26 per cent of extractive. The leaves of **Aniseed Buchu** (*B. pulchella*) are smaller than those of *B. betulina* and have an odor of citronella.

Rue (U. S. P. 1831 to 1882) is the leaves of *Ruta graveolens* Linné. The plant is a low shrub with fleshy leaves, 2- to 4-pinnatifid, and yellow flowers in terminal cymes. It has a strong, disagreeable odor, and a bitter, acrid, pungent taste. The leaves bear many short-stalked glands containing a very irritant volatile oil. The fresh leaves may blister the skin if applied or handled. The drug also contains rutin, a glycosidic coloring principle, also present in lemon peel, buckwheat leaves, black currant fruit, and other plants; it may contain or be related to vitamin "P," which is supposed to have an important effect on resolving arteriosclerosis and restoring the capillary function of assimilation.

Oil of Rue (U. S. P. 1873 to 1894) is obtained by steam distillation of the fresh leaves of *Ruta graveolens* L. It is of a yellowish or greenish color, darkens and thickens upon aging, and possesses the odor and taste of the leaves. It solidifies at about 10° C. It consists chiefly of methyl-nonylketone.

Fresh rue leaves and rue oil are irritants both externally and internally. In small doses, 65 mg., the oil is a stimulant, antispasmodic, carminative and an efficient anthelmintic. In larger doses it is an emmagogue and aphrodisiac. It has been used to produce abortion, but such doses are dangerous and narcotic poisonous.

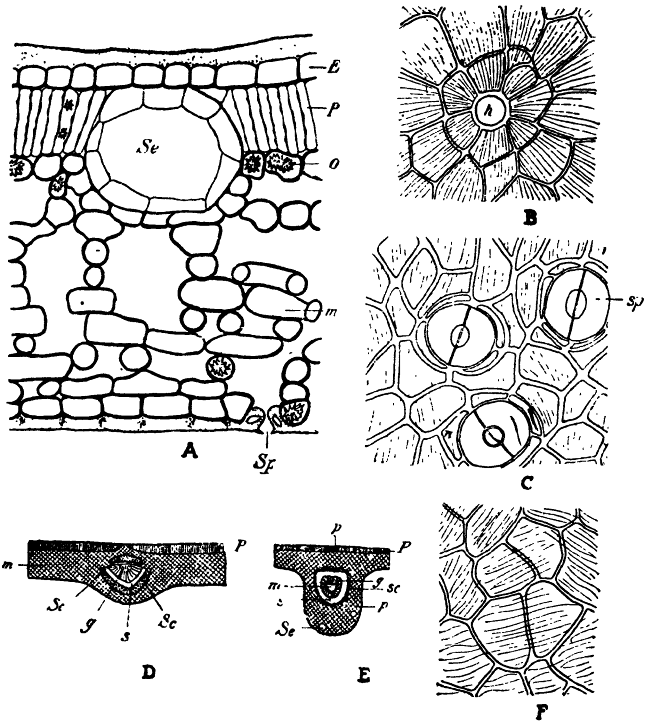


FIG. 197.—*Pilocarpus pinnatifolius: A*, Transverse section of lamina showing upper epidermis (*E*), oil cavities (*Se*), palisade cells (*P*), some of which contain rosette aggregates of calcium oxalate, loose parenchyma (*m*), some of the cells of which contain calcium oxalate (*o*), and lower epidermis with a stoma (*Sp*). *B*, Surface view of epidermis showing basal portion of a non-glandular hair (*h*). The basal remains of the hairs are often present, the upper portions being detached *C*, View of the under surface of the lamina showing stomata (*sp*). *D*, Diagram showing the arrangements of the tissues in one of the secondary veins: *P*, palisade cells; *m*, loose parenchyma; *Sc*, sclerenchyma; *s*, sieve; *g*, tracheæ. *E*, Transverse section of the primary or middle vein showing palisade cells (*P*), elongated parenchyma (*p*), oil glands (*Se*), sieve (*s*), tracheæ (*g*), which surrounds parenchyma (*m*), thus distinguishing it from the secondary vein. *F*, Surface view of upper epidermis of lamina. (After Meyer.)

Pilocarpus or Jaborandi (U. S. P. 1882 to 1916) consists of the leaflets of *Pilocarpus Jaborandi* Holmes (Pernambuco Jaborandi, 1894 to 1916); of *Pilocarpus microphyllus* Stapf (Maraham Jaborandi, 1905 to 1916); or of *Pilocarpus pinnatifolius* Lemaire (Paraguay Jaborandi, 1882 to 1894). The plants are shrubs indigenous to Brazil.

Pernambuco jaborandi is elliptical, lanceolate or oblong-lanceolate, 6 to 12 cm. in length, 1.5 to 4 cm. in breadth; summit obtuse, more or less emarginate; base rounded or acute, unequal; margin entire, slightly revolute; upper surface dark green or brownish green, glabrous; under surface yellowish or greenish brown, pubescent, with numerous light brown projections, midrib prominent;

glandular-punctate; texture coriaceous, brittle; odor slight; taste bitter, somewhat aromatic, becoming pungent.

Paraguay jaborandi is somewhat broader, sometimes obovate, thinner and less coriaceous and frequently with black disk-like fruits of a species of *Puccinia* on both surfaces.

Maranham jaborandi is smaller, coriaceous but rather thin, and frequently bearing the same *Puccinia* fruiting heads as found on Paraguay jaborandi.

The structure and powder are illustrated in Figures 197 and 198.

All of the commercial kinds of pilocarpus yield from 0.5 to 1 per cent of the alkaloid pilocarpine.

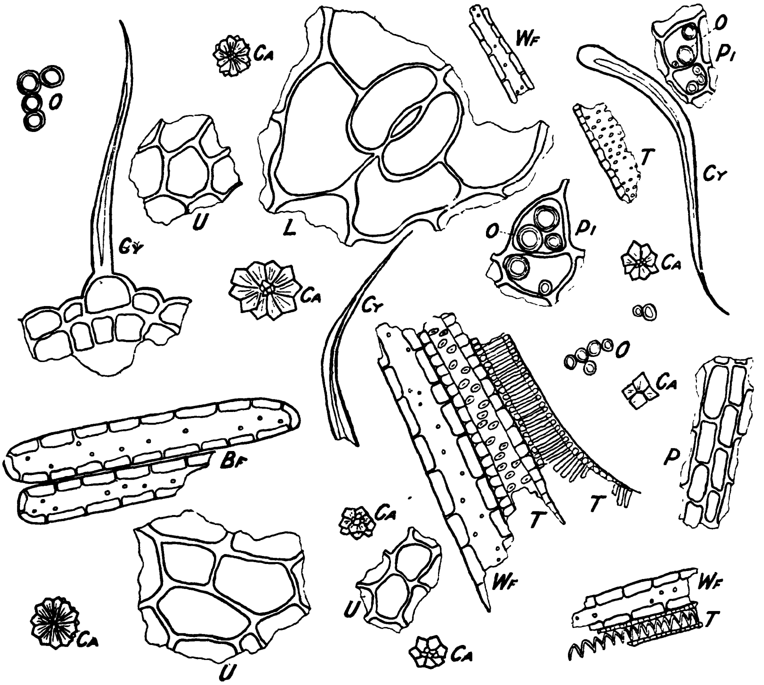


FIG. 198.—Powder of Pilocarpus. *U*, Fragments of upper epidermis; *L*, fragment of lower epidermis with a stoma; *Cy*, non-glandular hairs; *Ca*, rosette aggregates 10 to 27 microns in diameter; *Bf*, bast fibers; *Wf*, wood fibers; *T*, tracheæ with close annular thickenings and simple and bordered pores; *Pi*, parenchyma cells containing oil globules; *O*, oil globules; *P*, parenchyma cells. (Drawing by Haase.)

Pilocarpine Nitrate (U. S. P. 1905 to date) and **Pilocarpine Hydrochloride** (U. S. P. 1882 to 1936; N. F. 1936 to date) are salts of an alkaloid obtained from the dried leaflets of *Pilocarpus Jaborandi* Holmes, or of *Pilocarpus microphyllus* Stapf.

Pilocarpine is the lactone of pilocarpic acid, an acid having a glyoxaline nucleus. It is an oily, syrupy liquid, though its salts crystallize easily. It is usually obtained by treating the powdered leaves with sodium carbonate, extracting with benzene and then shaking the benzene extract with dilute hydrochloric or nitric acid. The aqueous solution is then made alkaline and shaken with chloroform; the chloroformic solution then shaken with acid and the alkaloidal salt allowed to crystallize.

Description and Tests.—Consult the U. S. Pharmacopœia and the National Formulary for the formulas and characteristics of these alkaloidal salts.

For the microchemical identification of pilocarpine the crystalline compounds with gold and platinum chloride are the only ones of value. The color test with hydrogen peroxide and potassium dichromate is, however, characteristic.

Uses and Dose.—The salts of pilocarpine are preferred to galenicals made from the drug. Pilocarpine is a diaphoretic, a sialagogue and a myotic. Average dose (nitrate or hydrochloride), 5 mg.

Xanthoxylum or Prickly Ash Bark (U. S. P. 1820 to 1926; N. F. 1926 to 1947) is the dried bark of *Zanthoxylum americanum* Miller, known in commerce as Northern Prickly Ash Bark (1820 to 1947); or of *Zanthoxylum clava-herculis* Linné, known in commerce as Southern Prickly Ash Bark (1873 to 1947). *Zanthoxylum* is from two Greek words, meaning yellow wood in reference to the color of the roots; *clava-herculis*, or Club of Hercules, is applied on account of the appearance of the cone-like cork-wings of the species. *Z. americanum* is a shrub or small tree indigenous from Quebec to Virginia and west to South Dakota, Nebraska and Kansas; *Z. clava-herculis* is a shrub or tree found south from Virginia to Texas.

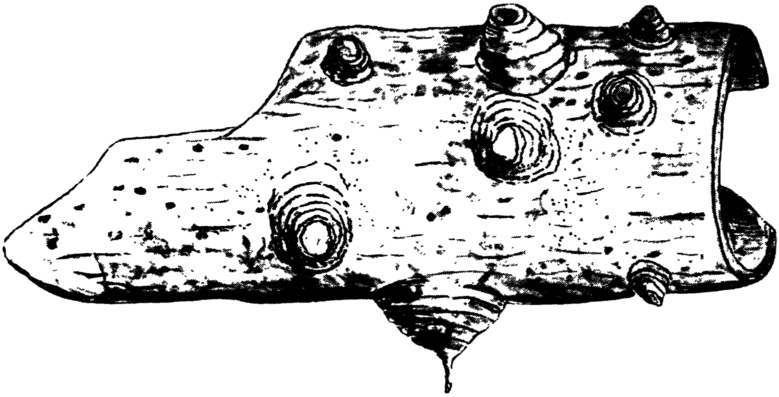


Fig. 199.—Southern Prickly Ash: A piece of the bark from commercial drug showing corky warts occasionally surmounted by a thorn. (Drawing by E. H. Wirth.)

The use of the bark as well as the berries dates back to the primitive medication of the Indians. It has been a domestic remedy since the days of the early settlers for the treatment of rheumatic affections, toothache and colic. The drug also enjoyed considerable favor among the Eclectics.

Prickly ash bark is in transversely curved or flattened pieces or in single quills, the bark 0.5 to 2 mm. in thickness (Northern), or up to 4 mm. in thickness (Southern); outer surface brownish gray to olive gray, or where cork is abraded, brownish or greenish; northern prickly ash bark may show lighter-colored lenticels, patches of foliaceous lichens, and radially flattened prickles; southern prickly ash bark shows large, conical projections of brownish cork up to 3.5 cm. in diameter, or scars where these have been knocked off. The inner surface is yellowish to light brown, finely striate longitudinally, and with minute flashing crystals (Northern) when viewed with a lens under a bright light, but mostly devoid of these crystals in Southern.

The powder is light yellowish brown; odor slight; taste bitter, acrid and pungent; starch grains numerous, nearly spheroidal, from 2 to 10 microns in diameter; calcium oxalate chiefly in monoclinic prisms from 10 to 45 microns in length, occurring in crystal fibers and in parenchyma cells of the primary cortex; oil-secretion cavities having a nearly colorless or light yellowish oil;

cork cells strongly thickened and lignified; bast fibers, thick-walled, slightly lignified, swelling perceptibly in hydrated chloral T.S.

In Southern prickly ash occur groups of large, more or less lignified stone cells, up to 150 microns in diameter and the lignified cork cells are more numerous.

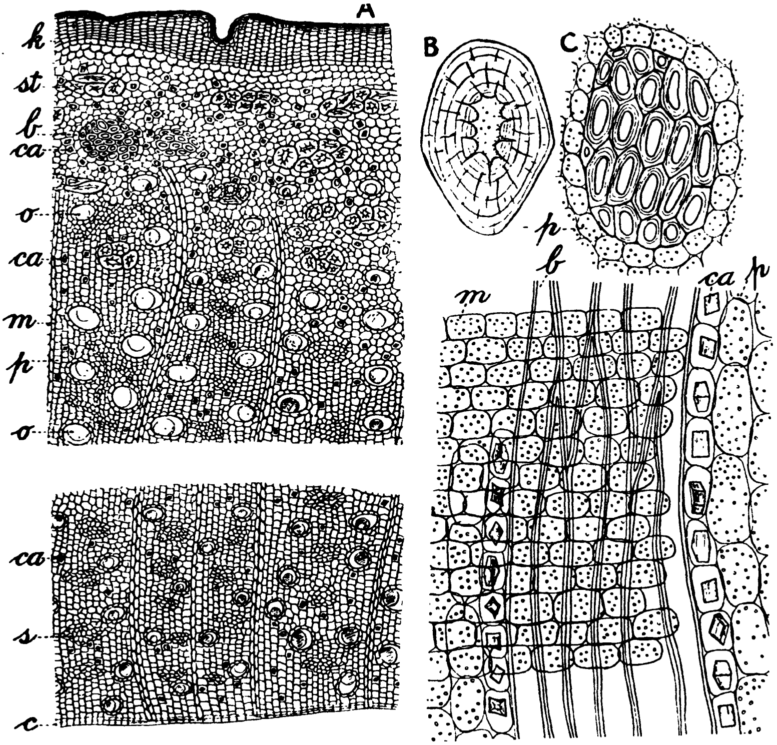


Fig. 200.—Southern Prickly Ash: *A*, Transverse section showing lignified cork (*k*) frequently in successive strata especially in the projections, the strata being separated by several rows of narrow tabular cells thickened on the tangential wall; a layer of collenchyma or parenchyma (*p*) containing starch and occasional calcium oxalate prisms (*ca*) and associated with groups of stone cells (*st*), bundles of primary bast fibers (*b*) and crystal fibers; in the inner bark, numerous light yellow oil-secretion reservoirs (*o*); strands of sieve tissue (*s*), medullary rays (*m*) 1 to 3 cells wide, and cambium (*c*). In northern prickly ash the lignified cork seldom exceeds 20 rows of cells, the collenchyma is more developed with thickened walls, and the stone cells are few. Scrapings from either the inner or outer surface show numerous rod-shaped crystals and flat prisms, up to 250 microns in length, which polarize light with a display of bright colors. *B*, Isolated stone cells showing pores and lamellæ. *C*, Group of bast fibers found in young, thin bark and surrounded by parenchyma (*p*). *D*, Longitudinal section near a group of bast fibers showing non-lignified bast fibers (*b*), calcium oxalate (*ca*) in crystal fibers, medullary ray (*m*), parenchyma (*p*) containing starch.

The drug contains two resins, one acrid, the other crystalline and bitter; an acrid volatile oil; a bitter alkaloidal principle, somewhat resembling berberine; a crystalline phenol compound, xanthoxylin; total ash, about 6 per cent; acid-insoluble ash, 0.3 per cent.

Xanthoxylum is a diaphoretic and an alterative. Average dose, 2 gm.

The bark of *Aralia spinosa*, see page 512 and Figure 201, is a common substitute of northern prickly ash bark. Southern prickly ash bark from which the corky cones have been removed by scraping has been substituted for northern prickly ash bark.

Xanthoxylum Fruit or Prickly Ash Berries (N. F. 1916 to 1947) is the dried full-grown fruit of *Zanthoxylum americanum* Miller, known in commerce as Northern Prickly Ash Berries, or of *Zanthoxylum clava-herculis* Linné known in commerce as Southern Prickly Ash Berries. The fruits are collected when full grown, and carefully dried.

The fruit consists of 2 to 3 follicles, 5 to 6 mm. in length, fleshy, gray-brown to black, more or less wrinkled, dehiscent along the ventral suture, and contain 1 or 2 subglobular, somewhat flattened, black, glossy seeds; odor aromatic; taste pungent and bitter. The powder is dark brown; the pericarp tissue showing large oil cavities and vascular tissues, surrounded by parenchyma cells containing irregular masses or sphere crystals of hesperidin; inner layer of pericarp of narrow, irregular, elongated cells with thick lignified walls; polygonal cells of the seed coat with dark brownish walls; numerous globules of volatile oil.

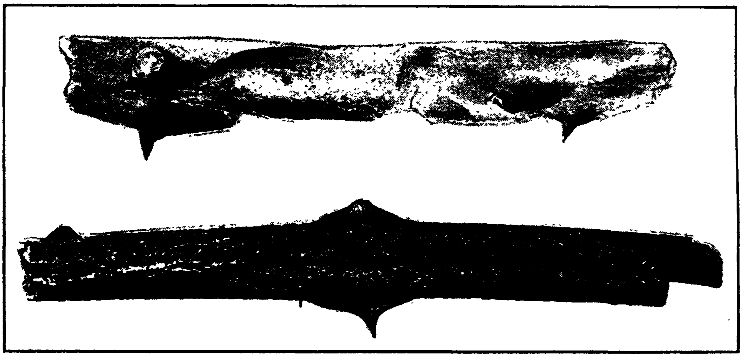


Fig. 201.—Northern Prickly Ash bark below, showing the longitudinally elongated spines; bark of *Aralia spinosa* above, with nearly circular spines.

Prickly ash berries contain a resin and a volatile oil, of which citral is one of the constituents. Total ash, 5.55 per cent; acid-insoluble ash, 0.13 per cent.

The drug is a tonic, a mild stimulant, a diaphoretic and an alterative. Average dose, 1 gm.

Angostura Bark, or Cusparia Bark (U. S. P. 1820 to 1882) is the bark of *Galipea officinalis*, a small tree growing abundantly in the mountainous districts of Venezuela. It was formerly used in the preparation of Angostura Bitters, which also contained gentian and a number of aromatic substances, as ginger, cinnamon, cardamom, orange or lemon peel, and caraway or cloves.

The bark occurs in quills or in transversely curved pieces, from 5 to 12 cm. in length, 2 to 3 cm. in width, and from 2 to 3 mm. in thickness; externally light yellowish or grayish brown, with occasional patches of a velvety porous cork; inner surface light brown and finely striate; fracture short, smooth and resinous; transverse surface of middle bark brownish red, inner bark brownish yellow with numerous shining resin canals and groups of bast fibers; odor distinct; taste bitter. Five alkaloids (cusparine, galipine, cusparidine, galipidine and cuspareine) have been isolated. Angostura is an aromatic bitter; it is a stimulant, a tonic and a stomachic. It is interesting to note that the bark ed *Strychnos nux vomica* has been substituted for angostura and has producof serious consequences, causing the use of angostura to be prohibited at one time in some countries. *S. nux vomica* is distinguished by a distinct line of stone cells separating the inner bark from the middle cortical layer.

Casimiroa Seed consists of the seeds of *Casimiroa edulis*, a tree widely distributed throughout Mexico and Central America. The fruit and seed of this tree are recognized by the Pharmacopœia of Mexico under the title of **Zapote Blanco.** The fruit is edible, although said to induce sleep, whereas the kernels of the seed have been regarded as deleterious or even fatal in their effects.

SIMARUBACEÆ, OR QUASSIA FAMILY

This family, which comprises about 30 genera and 150 species, consists chiefly of tropical or subtropical trees and shrubs, with alternate and pinnately compound leaves, regular flowers and drupaceous or samara-like fruits. Resin canals occur only in the peripheral region of the pith and are seldom found in the cortex. The hairs are usually both unicellular non-glandular and multicellular glandular. Calcium oxalate is usually secreted in the form of rosette aggregates or solitary crystals; in some instances styloids occur. *Alianthus glandulosa,* Tree of Heaven, is a commonly cultivated member of the family.

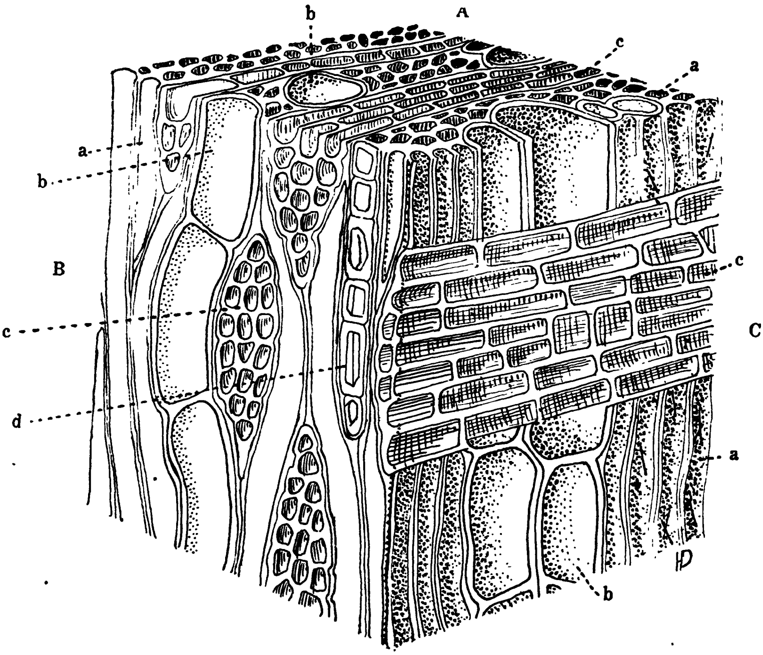


FIG. 202.—Jamaica Quassia. *a*, Wood fibers; *b*, tracheal tubes; *c*, medullary rays; *d*, wood parenchyma with prismatic crystals. The drawings (from *A*, transverse; *B*, tangential; and *C*, radial sections) are diagrammatically combined into a cube. (Drawing by Helen Day.)

QUASSIA

Quassia or Bitter Wood (U. S. P. 1820 to 1936; N. F. 1936 to date) is the wood of *Picrasma excelsa* (Swartz) Planchon, known in commerce as Jamaica Quassia, or of *Quassia amara* Linné, known in commerce as Surinam Quassia. *Quassia* is from *Quassi,* the name of a Surinam negro who first discovered the febrifuge properties of the drug; *picrasma* is

Greek meaning bitter; *amara* is Latin for bitter; and *excelsa* is from the Latin meaning surpassing, *i. e.*, the tallest tree in the genus. *Picrasma excelsa* is a tree attaining a height of about 25 meters, growing in the West Indies, while *Quassia amara* is a branching shrub or small tree attaining a height of 2 to 3 meters and found in Venezuela, northern Brazil and the Guianas. The wood is usually cut into logs (see Fig. 7) for shipment. "Quassia Cups" were formerly turned from the wood and the shavings used as the drug. The drug consists of chips, raspings or shavings. Quassia seems to have been used in Surinam as early as 1714 for the treatment of malignant fevers. The drug was at one time almost exclusively obtained from *Quassia amara* but now is largely derived from *Picrasma excelsa*.

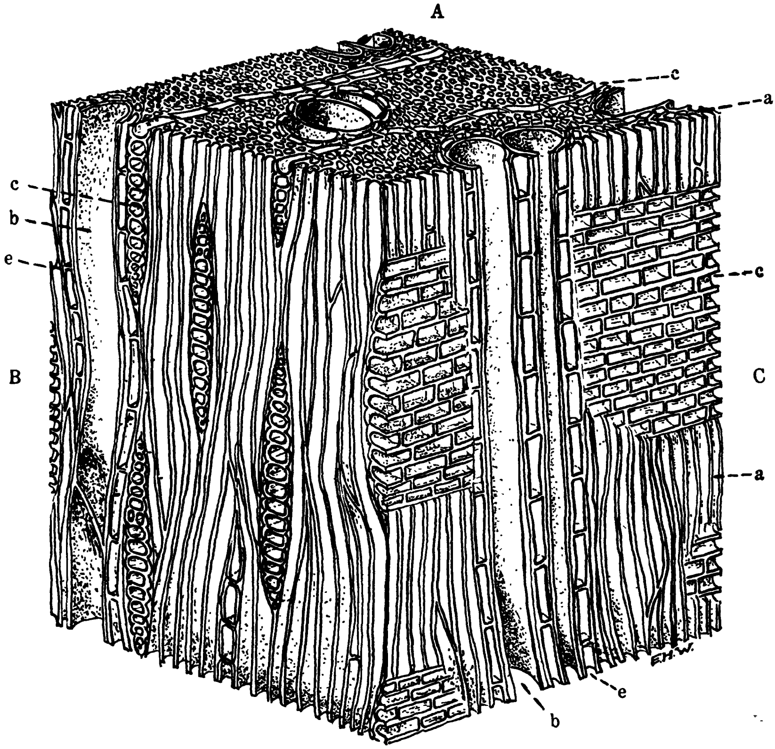


FIG. 203.—Surinam Quassia. *a*, Wood fibers; *b*, tracheal tubes; *c*, medullary rays. The drawings (from *A*, transverse; *B*, tangential; and *C*, radial sections) are diagrammatically combined into a cube. (Drawing by E. H. Wirth.)

DESCRIPTION AND STRUCTURE.—See Figures 202, 203, 204 and the National Formulary.

POWDER.—Light yellow; tracheal fragments with bordered pores; wood fibers long, thin-walled and with oblique simple pores; calcium oxalate in monoclinic prisms 6 to 30 microns in length or in sphenoidal microcrystals; starch grains few, spheroidal or ellipsoidal, 5 to 15 microns in diameter. When bark is present a few stone cells and cork cells are also found. In the bark of Surinam quassia stone cells are numerous.

CONSTITUENTS.—The drug contains up to 0.75 per cent of a bitter crystalline substance, quassin, which consists of two crystalline principles, *a*-picrasmin and *b*-picrasmin; an alkaloidal principle which gives a blue fluorescence in acidified alcoholic solution. Total ash, about 3.75 per cent; acid-insoluble ash, about 0.1 per cent.

USES AND DOSE.—Quassia is a bitter tonic. It is also used, in the form of an enema, as an anthelmintic. Average dose 0.5 gm.

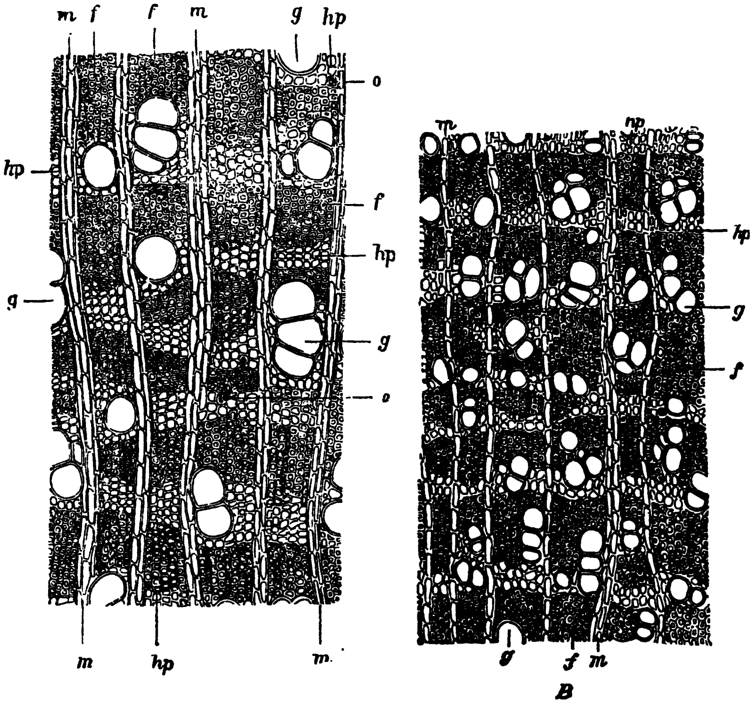


FIG. 204.—*A*, Transverse section of Jamaica Quassia. *B*, Transverse section of Surinam Quassia; *g*, tracheæ; *f*, wood fibers; *hp*, wood parenchyma; *o*, cells containing calcium oxalate; *m*, medullary rays. (After Meyer.)

Quassia Bark, the barks of *Picrasma excelsa* and *Quassia amara*, is used in medicine and probably contains principles similar to those found in the wood. The Surinam bark occurs in thinner, light-colored pieces and is sometimes admixed with the powdered drug. It is determined by the large stone cells. The wood of *Picræna quassioides* quite closely resembles Jamaica quassia in general appearance, microscopic structure and chemical constituents. Bitter principles are also found in other species of *Picrasma* and *Quassia*.

Simaruba Bark (U. S. P. 1820 to 1873) is the bark of the root of *Simaruba officinalis* and *S. amara*, stately trees, the former indigenous to northern Brazil, French Guiana and Guatemala, and furnishing the bark known commercially as **Orinoco Simaruba**; the latter growing in Panama, Guatemala, the Bahama Islands and Florida, and yielding the bark known as **Jamaica Simaruba.** The root bark is collected and deprived of the periderm. Most of the commercial supplies come from Ciudad Bolivar (Angostura) on the Orinoco River, Venezuela.

Orinoco simaruba occurs in flattened or transversely curved pieces, from 4 to 12 cm. in width, and from 2 to 5 mm. in thickness; externally grayish or yellowish brown, somewhat velvety to the touch, irregularly wrinkled, with occasional patches of the shining silvery periderm; inner surface yellowish brown, longitudinally striate; fracture short fibrous, porous and with yellowish stone cells; inodorous; taste very bitter and slightly aromatic.

Simaruba bark contains a volatile oil having an odor resembling benzoin; a non-volatile oil; a crystalline bitter principle, giving a violet color with sulfuric acid; a crystalline non-bitter substance; a fluorescent principle; a resin; gallic acid; and calcium oxalate and malate.

Simaruba is a bitter tonic.

BURSERACEÆ, OR MYRRH FAMILY

This family, comprising 13 genera and about 140 species, consists largely of tropical shrubs and trees, having alternate compound leaves and small flowers formed in racemes. The plants are especially distinguished by their internal secretory system. Schizo-lysigenous balsam canals or gum-resinous canals (Fig. 205) occur within the sclerenchymatous pericycle, also in the secondary cortex and medullary rays and occasionally in the primary cortex and pith. The epidermal layer in the leaves is usually modified to mucilage. The pericycle is a composite and continuous ring of sclerenchyma. The tracheæ as a rule have simple perforations, which are very large in the walls adjoining the parenchyma cells. The medullary rays are narrow. Calcium oxalate is secreted in the form of rosette aggregates or solitary crystals (Fig. 205). Glandular and non-glandular hairs are of a number of specific forms.

MYRRH

Myrrh or Gum Myrrh (U. S. P. 1820 to date) is an oleo-gum-resin obtained from *Commiphora abyssinica* (Berg) Engler or from *Commiphora molmol* Engler or from other species of *Commiphora.* The name Myrrh is from the Arabic *murr,* meaning bitter; *Commiphora* is from the Greek, meaning gum bearing; *molmol* is the native Somali name, and *abyssinica* refers to the habitat of the plants. The plants are small trees sometimes attaining the height of 10 meters and found growing in Arabia, Abyssinia, and Somaliland.

The gum-resin exudes naturally or from incisions made in the bark; it is first of a yellowish color, but soon hardens, in the intense heat of these countries, becoming darker, and is then collected. There are two principal commercial varieties of myrrh, the one known as **African or Somali Myrrh,** and the other as **Arabian or Yemen Myrrh,** the former being considered the better of the two.

There are numerous references to myrrh in the Old Testament, but it is highly possible that the product thus designated was one of the bdelliums. Myrrh was an ingredient of the embalming material of the Egyptians. Its use in incense and perfumes in ceremonial religious life since the days of remote antiquity is well known. Theophrastus, Pliny and other early writers mention it and from early times it has been valued in domestic medicine for its aromatic qualities.

DESCRIPTION.—In irregular, agglutinated tears or masses; externally rough and uneven, yellowish to reddish brown, covered with a yellowish dust; brittle, the fractured surface waxy, granular, oily, mottled, somewhat translucent in thin pieces; odor balsamic; taste aromatic, bitter and acrid.

POWDER.—In glycerin mounts the powder shows yellow or yellowish brown irregular fragments made up of a grayish matrix, containing oil globules, a few fragments of lignified tissues consisting of either sclerenchymatous fibers, or of small groups of stone cells, the individual cells of the latter having very thick, porous walls and being from 15 to 50 microns in length; and occasional starch grains from 10 to 35 microns in diameter and varying from spheroidal to somewhat pear-shaped grains.

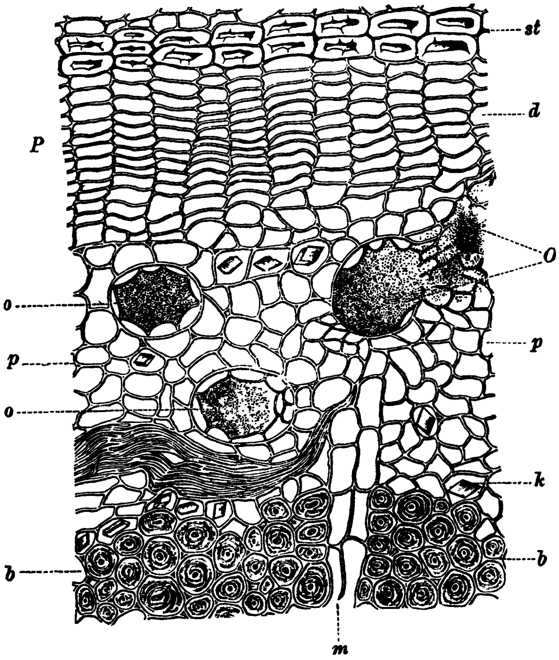


FIG. 205.—Transverse section of the bark of one of the *Burseraceæ*, probably *Commiphora myrrha: P*, borke made up of sclerotic cells (*st*) and cork (*d*); *o*, more or less spheroidal secretion canals, one of which (*O*) shows the irregular spreading of the gum-resin; *m*, medullary rays; *b*, bast fibers; *k*, crystals of calcium oxalate; *p*, parenchyma. (After Vogl.)

CONSTITUENTS.—A yellow or yellowish green, rather thick volatile oil, 2.5 to 8 per cent, having the characteristic odor of myrrh; resin, 25 to 40 per cent, composed of several constituents, among which are resin acids (α-, β- and γ-commiphoric acids), resenes and phenolic compounds, one of which yields protocatechuic acid and pyrocatechin; gum, about 60 per cent, consisting of soluble and insoluble portions and forming a mucilage that does not readily ferment; the gum is of the acacia type and yields arabinose as one of the products of hydrolysis; a bitter principle, sparingly soluble in water but soluble in alcohol; total ash, 5 to 13.4 per cent.

The volatile oil of myrrh consists of cuminol, about 1 per cent, eugenol, meta-cresol, pinene, limonene, dipentene and two sesquiterpenes. The acidity of old oil is due to free acetic, myrrholic and commiphorinic acids.

Standards and Tests.—Myrrh yields not less than 30 per cent of alcohol-soluble extractive and not more than 5 per cent of acid-insoluble ash.

Myrrh forms a brownish yellow emulsion when triturated with water (distinction from other gum-resins); an ethereal solution treated with bromine vapor becomes reddish (distinction from East Indian myrrh); when moistened with nitric acid it becomes purplish (distinction from false myrrh or bdellium).

Uses.—Myrrha is a stimulant and a stomachic. It is used frequently in mouth washes as an astringent.

Myrrh may be admixed with gums and other gum-resins, including several kinds of bdellium, which are obtained from various species of *Commiphora*, and which are characterized by not giving a purplish color with nitric acid. **African Bdellium** occurs in yellowish brown masses, reddish in transmitted light and with a pepper-like odor and bitter taste; **Indian Bdellium** occurs in irregular, reddish brown masses, covered with minute spicules of resin, and having a terebinthinate odor and an acrid taste; **Opaque Bdellium** occurs in yellowish, hard, opaque masses, with a faint odor and bitter taste, and the alcoholic solution of which is colored black with solutions of ferric chloride. Thin pieces of a bark are frequently present in opaque bdellium.

Bisabol, or East Indian Myrrh, is exported from eastern Africa and Asia; it resembles true myrrh, but an ethereal solution of it does not become reddish with bromine vapor. A solution of Bisabol, 1:15 in petroleum ether, gives a red zone when 6 drops of it are admixed with 3 cc. of glacial acetic acid and laid over 3 cc. of sulfuric acid; later the entire acetic acid layer assumes the same color. With genuine myrrh a very pale rose color forms.

Opopanax is a balsam-like product obtained from *Commiphora kataf*, a plant indigenous to Arabia, and is supposed to be the myrrh mentioned in the Bible. It yields from 6 to 10 per cent of a greenish yellow volatile oil with a pleasant balsamic odor; and also contains oporesinotannol (a compound not yielding umbelliferon on distillation) both free and combined with ferulaic acid; free ferulaic acid; vanillin, and a gum containing bassorin.

Mulu Kilavarv is a gummy exudation obtained from *Commiphora berryi*, a plant growing in India. It occurs in yellowish brown or dark brown translucent fragments, having a conchoidal, oily fracture, and consists chiefly of gum, with a small quantity of a tasteless resin and a volatile oil.

Olibanum or Frankincense is the oleoresin obtained from *Boswellia carterii* and **Manila Elemi** is obtained from *Canarium commune.*

MELIACEÆ, OR MAHOGANY FAMILY

This is a family numbering 37 genera and about 600 species of tropical and subtropical trees and shrubs, having mostly alternate and compound leaves and axillary clusters or racemes of flowers. The family is especially known for its yielding the mahogany wood, which is considered one of the most durable and valuable of cabinet woods. The **true mahogany** is obtained from *Swietenia mahagoni,* a native of tropical America and formerly very abundant in Jamaica; now, probably all of the mahogany wood comes from Central America. It is cultivated in Florida and California as an ornamental tree. Other genera of this family yield a wood which is substituted and sold for mahogany. Quite a number of timbers, obtained from plants entirely unrelated to the *Meliaceæ*, are also sold in commerce as mahogany.

Cocillana or Guapi Bark (N. F. 1916 to 1926) is the bark of *Guarea Rusbyi* (Britton) Rusby. Guarea is the native name, and the species is named after Dr. H. H. Rusby, who introduced the drug to medicine. The natives use it as an emetic; as an expectorant it resembles ipecac in its action on the respiratory organs.

The bark occurs in flattened or transversely curved pieces up to 2 cm. in thickness; externally grayish brown with whitish patches of a lichen, roughly and unevenly fissured, having longitudinal furrows and occasionally transverse fissures; inner surface brown, coarsely striate and often roughly fibrous from detached strands of bast fibers; fracture coarsely granular in the outer bark, and splintery fibrous in the inner bark; transverse surface with thick, light reddish brown periderm, having numerous slightly yellow stone cells, inner bark tangentially finely striate; odor slight; taste somewhat astringent, unpleasant and slightly nauseous.

Cocillana contains an alkaloid, rusbyine; a mixture of resins, 2.5 per cent; a fixed oil, 2.5 per cent; a caoutchouc-like substance; and tannic acid. Total ash about 7.5 per cent, acid-insoluble ash about 1.25 per cent. Cocillana is an expectorant and in large doses an emetic. Average dose, 1 gm.

Azedarach (U. S. P. 1820 to 1894) is the bark of the root of *Melia azedarach*, a beautiful shade tree indigenous to Asia, and cultivated in Europe and the southern United States. The drupaceous fruit is very astringent when green, yellow and sweet when ripe, and purplish-black on drying. It is poisonous to fish like cocculus, and to moths. The bark, preferably deprived of the periderm, occurs in quills or flattened pieces, 2 to 7 mm. in thickness; outer surface yellow or reddish brown; nearly smooth, with irregular lighter and darker patches; inner surface light brown, longitudinally striate and frequently with detached bast fibers; fracture short-fibrous; odor slight; taste sweetish, bitter and somewhat acrid.

The drug contains a resin with anthelmintic properties, which is insoluble in water but soluble in alcohol, ether, chloroform, carbon disulfide, petroleum benzine and oil of turpentine. It is precipitated from alcoholic solutions by the addition of water.

Azedarach is used mainly as an anthelmintic.

Indian Azadirach, Margosa or Neen Bark, is the dried bark of *Azadirachta indica*, a tree indigenous to the East Indies and rather widely distributed in the tropical countries of Asia and to some extent cultivated. The botanical name means "a noble tree of India." **Assam or Bangalore Gum** is obtained from this tree.

The bark contains a bitter alkaloid, margosine; a bitter amorphous resin; margosic acid; and tannic acid. Azadirach is used in India and the eastern colonies of Great Britain as a simple bitter, replacing gentian and quassia.

POLYGALACEÆ, OR MILKWORT FAMILY

This family consists of about 700 species, mostly herbs, except in the tropics where they may become shrubs and trees. The leaves are usually alternate and exstipulate, the flowers are perfect and irregular and the fruit is usually a capsule enclosing caruncled seeds. Among the histological features of this family the following may be mentioned. Only the transverse walls of the tracheæ are marked by simple pores. The wood fibers possess bordered pores, and the medullary rays are very narrow. The cells of the pith are sometimes lignified. In the leaves there are several important characteristics: (1) sclerotic cells are occasionally found in the loose mesophyll and palisade layer; (2) in *Polygala* there is a strong tendency for the epidermal cells to become papillose, thus resembling the leaves of *Erythroxylon;* and (3) terminal tracheids occur in the veins of *Polygala*. Non-glandular hairs are mostly unicellular, occasionally uniseriate. Glandular hairs are wanting.

SENEGA

Senega or Seneca Snakeroot (U. S. P. 1820 to 1936; N. F. 1936 to date) is the dried root of *Polygala senega* Linné. *Polygala* is from the Greek meaning "much milk" in reference to the early use of the plant

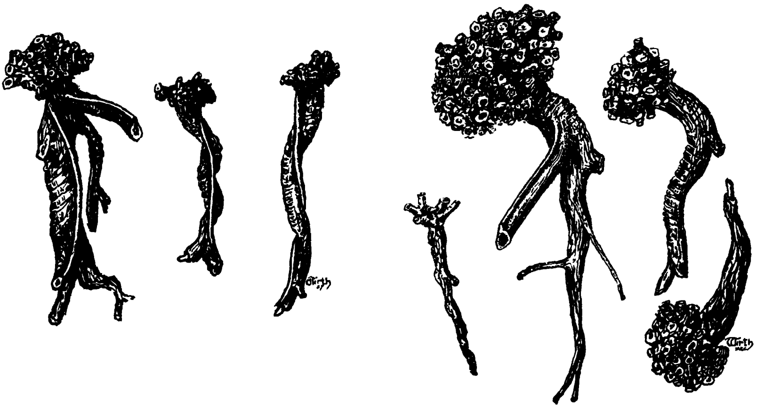


Fig. 206.—Senega: nearly entire, with broken and detached rootlets, crowned with numerous buds and short stem remnants, slenderly conical, more or less tortuous, somewhat branched 3 to 15 cm. in length, 2 to 10 mm. in thickness; externally dark yellow, the crown being rose-tinted, longitudinally wrinkled, slightly annulate, marked with circular scars of detached rootlets and in some cases by a keel, which is more prominent at the upper portion of the dried roots; side opposite keel more or less flattened; fracture short when dry, tough when damp; odor slight, penetrating; taste sweetish and acrid. (Drawings by Wirth.)

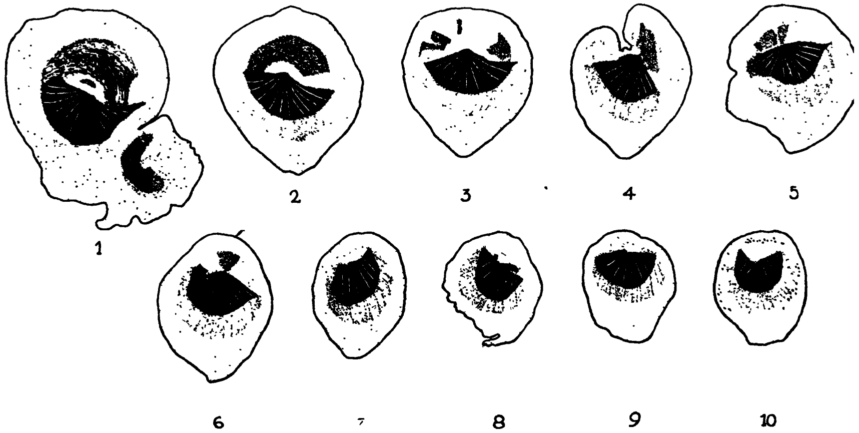


Fig. 207.—Senega: transverse sections cut through a root at equal intervals from tip to crown, showing the variation in the xylem in one root. The sections are elliptical or triangular, showing a characteristic excentral development of lemon-yellow wood, which varies in outline from elliptical or ovate to irregularly fan-shaped, due to the presence of one or more broad medullary rays, and is surrounded by an unevenly developed dark yellow cortex which is thickest outside the broadest strands of wood, and forms the keel on drying. (Drawings by Carpenter; courtesy of the Journal of the Amer. Pharmaceutical Assn.)

as a galactagogue; *senega* refers to the Seneca tribe of North American Indians. The plant is an herbaceous perennial with a large knotty crown from which several leafy stems up to 30 cm. high arise in the spring and die down in the fall. The roots are dug in the fall and carefully dried. There are two commercial varieties, the Northern, collected in Manitoba and Minnesota; the Southern, from Virginia to Texas.

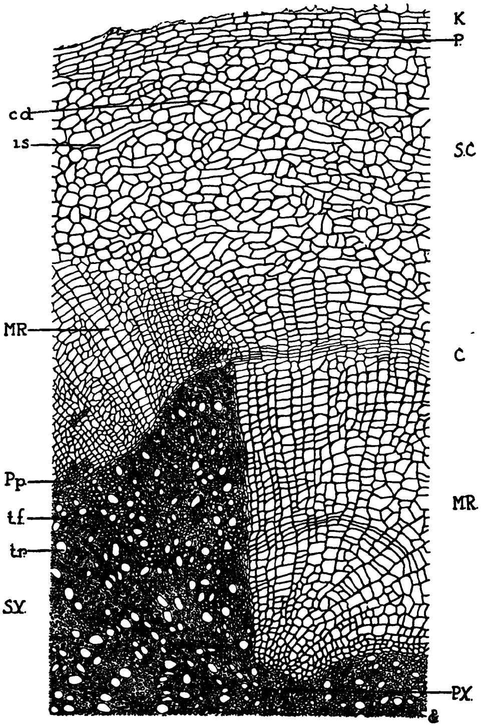


FIG. 208.—Senega: transverse section of the root showing an outer layer of several rows of yellowish brown cells (*K*), a phellogen (*P*), a secondary cortex (*SC*) showing occasional intercellular spaces (*is*) and groups of cells undergoing active cell division (*cd*); an inner bark composed of small groups of sieve tissue (*Pp*) associated with parenchyma and alternating with medullary rays (*MR*) one to three cells wide. The parenchyma of the cortex, phloem and medullary rays have amorphous contents which form oily drops upon the addition of potassium hydroxide T.S. or chloral T.S. The secondary xylem (*SV*) shows fiber tracheids (*tf*) and tracheal tubes (*tr*). The primary xylem (*PX*) may be seen at the center of the root. (Drawing by Paul D. Carpenter; courtesy of the Journal of the Amer. Pharmaceutical Assn.)

Senega was used by the Indians as a remedy for snake bite, was investigated by early American physicians, was known in Europe in 1738, and as one of the new American drugs, enjoyed a very early reputation as an expectorant and cough remedy.

DESCRIPTION AND STRUCTURE.—See Figures 206, 207 and 208.

POWDER.—Pale brown to weak yellow; odor suggesting methyl salicylate; somewhat sternutatory; taste sweetish, becoming strongly acrid; fragments may show thin walled parenchyma, cork-like cells, sieve tissue, narrow tracheæ, short pointed tracheids with numerous simple or bordered pores, lignified medullary ray cells with simple pores.

Constituents.—About 5 or 6 per cent of two glucosides: senegin, which resembles saponin, and polygalic acid, which is sternutatory; 0.12 per cent of a volatile oil which is chiefly methyl salicylate; resin; pectin; sugar; and considerable proteins. Total ash, from 2.4 to 4 per cent; acid-insoluble ash, from 0.35 to 1.65 per cent.

Uses and Dose.—Senega is an expectorant, a stimulant and an irritant. Average dose, 1 gm.

Polygala Rubella or Bitter Polygala (U. S. P. 1820 to 1882) is the dried root and herb of *Polygala rubella.* It is a biennial herb about 20 cm. high, growing in dry fields from Canada to the Gulf of Mexico. The leaves are alternate, linear-oblong, on simple stems terminated by a narrow raceme of purple, pendulous flowers. The drug is odorless and bitter in taste. It contains a very bitter principle and has some value as a bitter tonic.

Saponin-like substances are found to a greater or less extent in other species of *Polygala,* of which at least forty have been used in medicine. *Polygala alba,* yielding **White Senega,** contains saponins and a normal wood. Other genera of *Polygalaceæ* seem to have constituents similar to Senega, as *Comesperma* of Australia and *Monnina* of South America.

The roots of *Polygala angulata* are collected in Brazil, and are commonly known as **White Ipecac or Poaya Blanca.** The roots resemble those of senega, but are from 7 to 20 cm. in length and from 1 to 9 mm. in diameter. They are nearly cylindrical, more or less tortuous, light brown in color, longitudinally wrinkled and marked by numerous transverse fissures. The crown is surmounted with a number of stem-bases which somewhat resemble the roots. They probably contain saponin, and on this their emetic properties depend.

EUPHORBIACEÆ, OR SPURGE FAMILY

This is a large family of about 4000 species, which are widely distributed. Outside of the fact that the flowers are subtended by an involucre, which resembles a calyx, and the fruit is a 3-lobed capsule, there are no distinctive morphological features which extend throughout all members of this family. It is ordinarily stated that the plants possess a milky acrid juice, but this is only true of some of the genera. There are many different kinds of secretory tissues in this family: (1) **Lacticiferous tubular cells** are especially characteristic of Euphorbia. They occur in the pith, cortex, and in the veins of the leaves, and the milky contents may contain starch grains, protein crystals, rosette aggregates of calcium oxalate and tannin. (2) **Lacticiferous vessels** occur in *Hevea,* one or more species of which yield caoutchouc, and in *Manihot,* the tuberous roots of which furnish tapioca starch. In the former the juice is of a milky character and in the latter in the nature of a watery sap. (3) Rows of **laticiferous sacs** are confined to the genus *Micrandra.* The cells form long chains and contain a sap, which, on drying, is colored gray. (4) **Tanniferous cells** occur singly or in chains and have a brownish content. They are widely distributed in the *Euphorbiaceæ.* (5) A secretory organ, consisting of very much **elongated sacs** having a brownish content, is found solely in the pith cells of *Mallotus* and some other genera. It is usually surrounded by a ring of small cells resembling an epithelium. (6) **Idioblasts,** or secretory cells with an oleoresin content, are found in *Ricinus*, *Croton*, etc. The cells are large and contain a yellowish and strongly refractive secretion, giving rise to transparent dots in the leaves. (7) **Secretory lacunæ**, resembling the intercellular secretory receptacles, occur in some of the *Euphorbiaceæ*. (8) **Mucilage Lacunæ**, or groups of cells having mucilaginous walls, are found in a limited number of genera. Both glandular and non-glandular hairs occur in a number of specific forms. Stinging hairs are also found in a number of tropical genera.

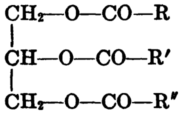
FIXED OILS, FATS AND WAXES

Fixed oils, fats and waxes are mixtures of esters of aliphatic acids. In fixed oils and fats the alcohol is glycerol while in waxes a large number of higher straight-chain alcohols have been found.

Fixed Oils and Fats differ only as to melting point; those that are liquid at normal temperatures are known as *fatty* or *fixed oils* while those that are semisolid or solid at ordinary temperatures are known as *fats*. Also, there is no chemical difference between fats and oils of plant or of animal origin. While most vegetable oils are liquid at ordinary temperatures and most animal fats solid, there are nevertheless notable exceptions such as cocoa butter, a solid vegetable oil and cod-liver oil, a liquid animal fat. There is considerable evidence that fats are synthesized from carbohydrates. Many fat-containing moulds and yeasts can be grown on culture media containing glucose, and in the animal kingdom the fattening of hogs on corn, both bear evidence in support of this theory. In general also, the formation of fats in seeds is preceded by carbohydrate storage.

Vegetable oils and fats may occur in various parts of the plant but as a general rule seeds contain larger quantities of fats and oils than do other plant parts. Seeds are the usual sources of fixed oils and as a few examples the following might be mentioned: cottonseed, linseed, sesame seed, hemp seed, coconut, castor beans, almond, etc. In a few instances other plant parts may yield considerable quantities of fixed oil (pericarp of the olive). In certain fungi (*e. g.*, ergot) fat is the characteristic reserve food material.

Chemically, the fixed oils and fats are glycerides of fatty acids having the general formula:



$$\begin{array}{l}CH_2\text{—}O\text{—}CO\text{—}R\\ |\\ CH\text{—}O\text{—}CO\text{—}R'\\ |\\ CH_2\text{—}O\text{—}CO\text{—}R''\end{array}$$

If R, R′ and R″ are the same fatty acid radical the compound is called triolein, tripalmitin, tristearin, etc., as the case may be. If R, R′ and R″ are different fatty acids a mixed glyceride results. The composition of the glycerides in any fixed oil or fat is influenced by the amounts of various fatty acids present at the time of formation. Thus it will be seen that the composition of fixed oils and fats from any source may vary within certain limits.

It is usually true that the glycerides of unsaturated fatty acids are liquid while the glycerides of saturated fatty acids of sufficient chain length are solid.

The predominance of either type in an oil will determine whether the mixture is liquid or solid. Some of the more common fatty acids are:

Caproic	$CH_3(CH_2)_4COOH$
Caprylic	$CH_3(CH_2)_6COOH$
Capric	$CH_3(CH_2)_8COOH$
Lauric	$CH_3(CH_2)_{10}COOH$
Myristic	$CH_3(CH_2)_{12}COOH$
Palmitic	$CH_3(CH_2)_{14}COOH$
Stearic	$CH_3(CH_2)_{16}COOH$
Arachidic	$CH_3(CH_2)_{18}COOH$
Oleic	$CH_3(CH_2)_7CH:CH(CH_2)_7COOH$
Linoleic	$CH_3(CH_2)_4CH:CHCH_2:CH(CH_2)_7COOH$
Linolenic	$CH_3CH_2CH:CHCH_2CH:CHCH_2CH:CH(CH_2)_7COOH$
Ricinoleic	$CH_3(CH_2)_5CHOHCH_2CH:CH(CH_2)_7COOH$

Fixed oils are sometimes classified into drying oils, semi-drying oils and non-drying oils. This classification is based upon their ability to absorb oxygen from the air. This oxygen saturates the double bonds to form oxides which may polymerize to form hard films. This property of drying oils is of great importance in the paint industry. The double bonds in the unsaturated fatty acids will also take up hydrogen under the proper conditions. Hydrogenation of the liquid oils will produce semi-solid fats which find extensive use as cooking-fats and shortenings.

The United States Pharmacopœia and the National Formulary include several tests for fixed oils, by means of which their identity, quality and purity may be determined. These tests are based upon the chemical constitution of the fatty acids. Thus the acid value or acid number indicates the amount of free fatty acids present in the oil; the saponification value indicates the amount of saponifiable matter present, including the amount of free fatty acids, the nature of the fatty acid radicals and the amount of mono-, and di-glycerides present; and the iodine number indicates the degree of unsaturation. Other physical constants such as melting point, specific gravity and refractive index also serve as identity, purity and quality tests.

Fixed oils and fats of vegetable origin are obtained by expression in hydraulic presses. If the expression is carried out in the cold the oil is known as a "virgin oil" or a "cold pressed oil" in contrast to a "hot pressed oil" in the preparation of which heat is used. Sometimes organic solvents are used for the extraction of the oils. Animal fats are separated from other tissues by rendering with steam, with or without pressure. The heat melts the fat which rises to the top and may be separated by decantation. Oils may be further clarified by filtration and bleached with ozone. Stearins are often removed by chilling and filtration.

Fixed oils and fats are employed in pharmaceuticals for their emollient properties. As ointments or as liquid (liniments) or solid (creams) emulsions, they may also be used as vehicles for other medicaments. A few, such as castor oil and chaulmoogra oil, have special therapeutic properties. In the arts and in industry they are used in the manufacture of soaps (sodium and potassium salts of the fatty acids), as drying oils in the manufacture of paints and varnishes and as lubricants. Fats also form an important class of foods.

One property of fixed oils and fats which can bear mention because it differentiates them from volatile oils, is the fact that fixed oils and fats leave a permanent stain on paper.

Waxes are usually defined as esters resulting from the condensation of high molecular weight straight-chain acids and high molecular weight, primary, straight-chain alcohols. Such esters, of course, exist in waxes, but in reality waxes are better defined as mixtures of different molecular weight acids and alcohols. In addition waxes may also contain paraffins.

In plants, waxes are found in connection with the outer cell walls of epidermal tissue, particularly in fruits and leaves, where the function appears to be protection against the penetration or loss of water. Insects also secrete waxes, for various purposes. Carnauba wax (*Copernicia cerifera*) and bayberry wax are examples of vegetable waxes and Lac Wax and Beeswax are examples of insect waxes.

Waxes are employed in pharmaceuticals for "hardening" ointments and cosmetic creams and in the preparation of cerates. In industry and the arts they are used for protective coatings.

CASTOR OIL

Castor Bean or Castor-oil Seed (U. S. P. 1831 to 1842) is the ripe seed of *Ricinus communis* Linné. *Ricinus* is the Latin for a tick or a bug, applied because the seed resembles some bugs in shape and markings.

The plant is an annual in temperate climates to a tree, attaining the height of 15 meters, in the tropics. There are many forms of the plant with variations in the shape of the leaves, and the color, size and markings on the seeds. The fruit is a 3-celled spiny capsule, each cell containing an ovoid albuminous seed. The plant is indigenous to India. It is extensively cultivated in India, South America, the Levant, various parts of Africa, the East and West Indies, southern Europe and southern United States. The seeds have been found in Egyptian tombs. The oil appears to have had only technical use until the eighteenth century when its medicinal use began.

The seed is anatropous, elliptical-ovoid, somewhat compressed, from 8 to 18 mm. in length, and from 4 to 7.5 mm. in thickness; externally mottled grayish and brown, varying considerably in color, smooth, with a prominent whitish caruncle at the somewhat pointed end, from which the raphé extends, on the flat or ventral side, to the chalazal end; seed coat thin, brittle; endosperm large, white, oily and bearing two thin foliaceous cotyledons, one on either side of a central, lenticular cavity, and connected with the short caulicle and radicle, the latter directed toward the micropile. (See Figure 209).

Castor Oil (U. S. P. 1820 to date) is the fixed oil obtained from castor beans.

Castor Oil is prepared by passing the seeds through a decorticator having rollers with sharp cutting edges which break the testas, but do not injure the kernel; separating the testas by means of sieves and compressed air; and subjecting the kernels to pressure. The oil is steamed to destroy albumins, filtered and bleached. The yield of this "cold pressed" oil is about 35 per cent. The oil cake is steamed and a second expression is made which yields an oil of inferior quality.

CONSTITUENTS.—Principally triricinolein; also isoricinolein, palmitin and dihydroxystearin; free ricinoleic acid, and its isomer, produced by hydrolysis in the duodenum are the cathartic principles. The seeds contain from 45 to 55 per cent of fixed oil; about 20 per cent of protein substances, consisting of globulin, albumin, nucleoalbumin, glycoprotein and ricin (a toxalbumin); an alkaloid, ricinine; several ferments; an ester composed of methyl alcohol and ricininic acid; sugar; a bitter principle; resin; and gum. The seed coat yields 10 per cent of ash; the kernel about 3.5 per cent. The toxalbumin, ricin, is not removed in the extraction of the castor oil, but remains in the **Oil Cake**. It is very poisonous to cattle, but does not affect poultry.

DESCRIPTION.—Pale yellowish or almost colorless; transparent; viscid; odor faint and mild; taste bland, slightly acrid and usually nauseating. Consult the U. S. Pharmacopœia for constants and tests.

USES AND DOSE.—Purgative. Average dose, 15 cc. It is also employed in the manufacture of soaps and as a lubricant for internal combustion engines.

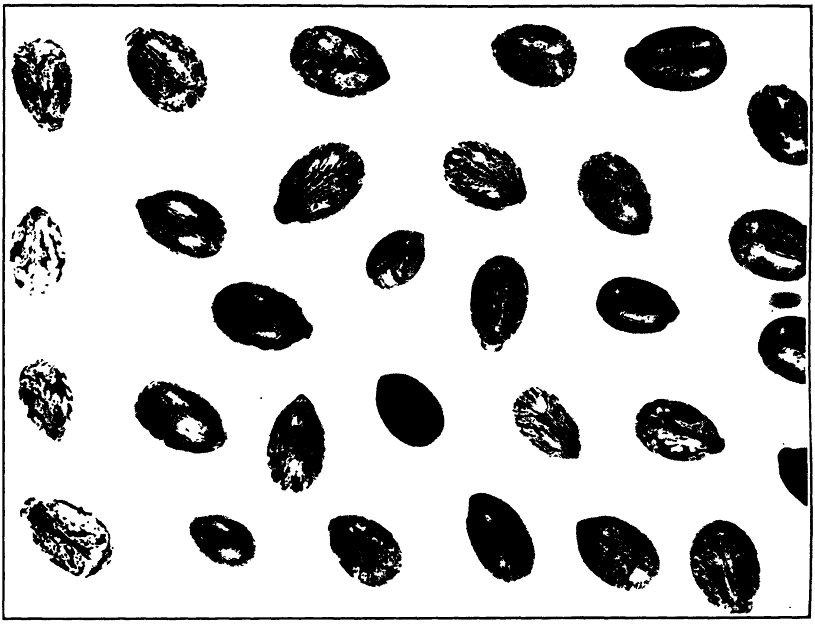


FIG. 209.—Castor Beans. (Photo by Adamson.)

Hydroxystearin Sulfate or Sulfated Hydrogenated Castor Oil (N. F. 1947 to date) is a substance prepared by sulfating partially hydrogenated castor oil.

Fixed oils may be **hydrogenated** by passing hydrogen, in the presence of nickel or palladium through the oil heated to 160° to 200° C. The unsaturated glycerides are more or less completely converted to saturated glycerides, which are solid at room temperature and very stable. Many such oils are used for culinary purposes.

Sulfated or Sulfonated Oils are obtained by reacting sulfuric acid with the oil, keeping the temperature down by chilling. The oil is then washed and neutralized. If the oil contains an ethylene linkage, the acid molecule adds on to the double bond; if the oil be hydrogenated, the hydroxyl group reacts with the acid to form water. The compound form is a sulfate of the fat.

DESCRIPTION.—Hydroxystearin sulfate is a pale yellow brown, semi-soft, unctuous mass having a faint odor. It is miscible with water, alcohol, glycerin, propylene glycol, fixed oils and the petrolatums in all proportions. It is acid to litmus with a pH of 6.1 to 6.5, and contains up to 25 per cent of moisture. For other constants and tests see the National Formulary.

STANDARDS.—Hydroxystearin sulfate, on a moisture-free basis, contains not less than 8.5 per cent and not more than 9.5 per cent of organically combined sulfur trioxide.

USES.—Medicinally in water-absorbent (hydrophilic) ointments, creams and pastes.

Riodine (NNR) is a 66 per cent solution in oil of an iodine addition product of castor oil. It contains about 17 per cent of iodine and is used as a substitute for the inorganic iodides. The dose is 0.4 to 1.2 gm. per day.

Croton Oil (U. S. P. 1831 to 1936; N. F. 1936 to 1947) is the fixed oil expressed from the seed of *Croton tiglium* Linné. *Croton* is from the Greek, meaning a tick or bug, and is used because the seed resembles a bug in shape; *tiglium* is from the Greek, meaning "to have a thin stool."

The plant is a small tree indigenous to tropical Asia and cultivated in India, Ceylon and the East Indies. The seeds resemble castor seeds in size and shape, but are dark brown in color. The kernel contains about 50 per cent of a fixed oil which is expressed by methods similar to those employed in obtaining castor oil. Besides the oil, the seed also contains a very toxic albuminous substance, crotin, a mixture of croton globulin and croton albumin, and comparable to ricin. Croton oil is produced in India and also in Europe. The ancient Hindu physicians were not acquainted with the use of the drug, which appears to have originated in China. Croton was introduced into Europe by the Dutch during the sixteenth century. Its use appears to have experienced periods of favor and disfavor.

Croton oil is a pale yellow or brownish yellow, somewhat viscid and slightly fluorescent liquid, with a faint characteristic odor. Croton oil is composed of the glycerides of the following acids: stearic, palmitic, myristic, lauric, oleic, tiglic, acetic, butyric, formic, and valeric. Croton oil is acid to litmus paper which has been moistened with alcohol. It forms a clear solution on heating with twice its volume of dehydrated alcohol and more or less completely separates on cooling. A mixture of 1 part nitric acid, 1 part distilled water and 2 parts croton oil, when shaken and allowed to stand, does not solidify. Its saponification value is not less than 200 and not more than 215; its iodine value not less than 104 and not more than 110.

USES AND DOSE.—Croton oil is a drastic purgative. It is usually administered on sugar or bread crumbs. Average dose, 0.06 cc. It is the most violent of all purgatives and one of the most powerful local irritants.

Caution should be observed in handling croton oil as it causes pustular eruptions when applied to the skin.

Physic Nuts or Purging Nuts are the seeds of *Jatropha curcas*. The seeds are more or less oval, black and from 15 to 20 mm. in length. They contain about 20 per cent of a fixed oil and a substance comparable with ricin, known as curcin. Both oil and seeds are powerful purgatives. The bark of the tree, *Croton gubouga*, a species widely spread in Nyasaland, Rhodesia and Portuguese East Africa, is known as **Transvaal Croton Bark.** In external appearance the bark is 2 to 3 mm. thick, generally gray in color, with corky warts or longitudinal bands of cork. The bark possesses a persistently acrid, somewhat numbing taste.

The entire plant of *Cluytia similis*, indigenous to South Africa, is reputed to be of value as an antidote for anthrax and for the disinfection of anthrax-infected meat, while the root is stated to be eaten by some of the natives as an antidote for snake-bite poisoning.

Stillingia or Queen's Root (U. S. P. 1831 to 1926; N. F. 1926 to 1947) is the dried root of *Stillingia sylvatica* Linné. *Stillingia* was applied in honor of Dr. A. B. Stillingfleet, an English botanist; *sylvatica* means wood-loving, in reference to the habitat of the plant.

The plant is an herbaceous perennial growing in sandy soil from Virginia to Florida and west to Texas. The roots are collected in August, deprived of the rootlets and sometimes cut into transverse or longitudinal slices and carefully dried. Stillingia was used by the early settlers of the South in domestic medicine as a purgative and alterative. It has been a constituent of several popular remedies. Since 1860 it has been employed both empirically and by the medical profession.

Stillingia root is usually in pieces, 5 to 30 mm. in diameter; externally dark brown, longitudinally wrinkled, rootlets or scars few; internally cork thin, lignified, reddish brown; bark up to 4 mm. thick, soft, spongy, easily separable from the wood, with starch-bearing parenchyma and numerous resin and tannin cells; bast fibers long and narrow with thickened, slightly lignified walls; xylum of thin-walled, slightly lignified tracheids, with occasional strands of tracheæ; medullary rays 1 or 2 cells wide; starch grains numerous, 5 to 45 microns in diameter, mostly single and spheroidal, with a central cleft; occasional rosette aggregates of calcium oxalate up to 70 microns in diameter; odor faint; taste bitter, acrid and pungent.

CONSTITUENTS.—Stillingia contains a volatile oil, from 3 to 4 per cent; an acrid resin, sylvacrol; an acrid fixed oil; 10 to 12 per cent of tannin; starch; calcium oxalate. Total ash, 4.23 per cent; acid-insoluble ash, 1.2 per cent.

Stillingia which has been stored for more than two years must not be used. Stillingia is an alterative and is usually combined with other drugs. Average dose, 2 gm.

Euphorbia Pilulifera, Euphorbia, or Pill-bearing Spurge (N. F. 1916 to 1947) is the dried plant of *Euphorbia pilulifera* Linné. *Euphorbia* is the Greek name of an African plant, named for Euphorbus, physician to King Juba; *pilulifera* means pill-bearing, alluding to the shape of the fruit. This is an annual herbaceous plant found growing in most tropical and sub-tropical countries. It is common in the United States from Texas to Arizona. Most of the commercial supply, however, comes from India. The plant is gathered at the time of flowering or fruiting and carefully dried.

For the description of the whole drug and of the powder see the National Formulary, seventh edition.

The drug contains an alkaloid, 0.1 per cent; a glucosidal substance, several resins, tannic acid, mucilage, sugar, protein. Total ash, about 4 per cent; acid-insoluble ash, about 0.5 per cent. The drug has some reputation as an anti-asthmatic. Average dose, 2 gm.

Euphorbia Corollata or Large-Flowering Spurge (U. S. P. 1820 to 1882) is the root of *Euphorbia corollata.*

Euphorbia Ipecacuanha or Ipecac Spurge (U. S. P. 1820 to 1882) is the root of *Euphorbia ipecacuanha.*

The plants are herbaceous perennials producing stems up to 2 meters in height from the crowns of large branching roots. They are indigenous to the eastern United States from Canada to Florida, *E. corollata* more to the north, and *E. ipecacuanha* more to the south, and prefer dry sandy habitats. The drugs are extracted with water and alcohol. In doses of 1 to 2 gm. they are actively emetic; in smaller doses they are brisk purges; in doses of 0.5 gm. they are diaphoretic and expectorant. The marked purging powers and the tendency to produce nausea have handicapped the drugs as emetics and cathartics, and they have been supplanted with other medicines.

Euphorbium is a dried resinous latex obtained from *Euphorbia resinifera,* a cactus-like plant growing in Morocco. The Arabs make incisions in the stems from which the latex flows abundantly in the rainy season. The latex solidifies on the plant and finally falls to the ground. The drug occurs in dull light brown tears and is used to some extent as a vesicant in veterinary practice.

KAMALA

Kamala, Rottlera or Glandulæ Rottleræ (U. S. P. 1863 to 1905; N. F. 1936 to date) consists of the hairs obtained from the capsules of *Mallotus philippinensis* Muller Argoviensis. *Mallotus* is Greek meaning woolly or fleecy: the young branches, leaves and capsules are covered with fine hair. The plant is an evergreen shrub indigenous to southeastern Asia and widely distributed throughout tropical Asia, Australia and the Philippines. The glandular hairy capsules are thrown into large baskets, rolled about and rubbed to remove the hairy covering. This impure powder is passed through a sieve to remove the larger fragments and tissues, other than the hairs. Most of the commercial supplies are exported from Indo-China to London, whence they are distributed.

DESCRIPTION.—A fine, granular, brownish red powder, consisting of yellowish red, glandular hairs and grayish, stellate non-glandular hairs; also a small quantity of vegetable tissues. Also see Figure 210.

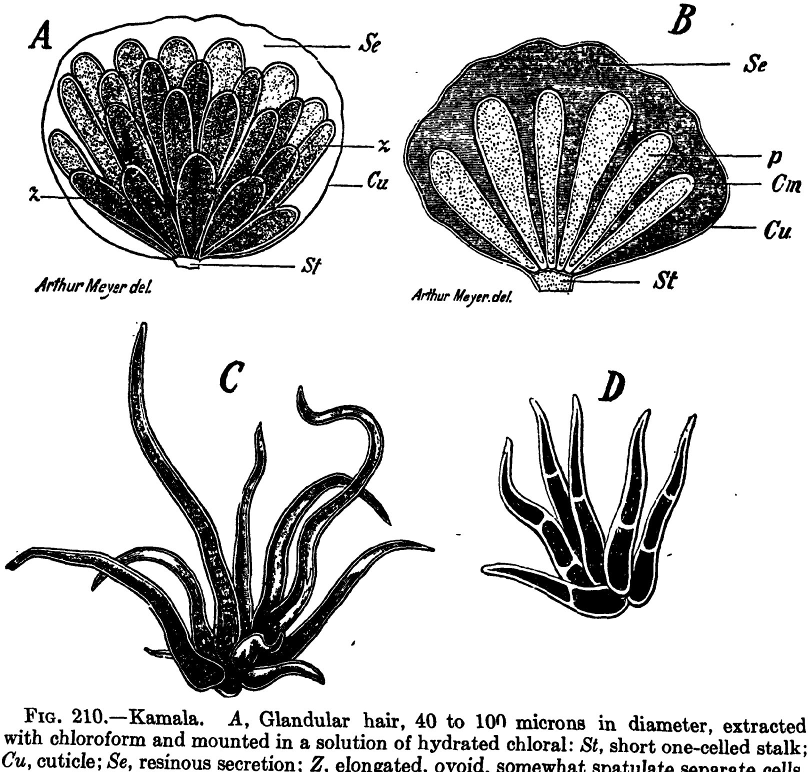


FIG. 210.—Kamala. *A*, Glandular hair, 40 to 100 microns in diameter, extracted with chloroform and mounted in a solution of hydrated chloral: *St*, short one-celled stalk; *Cu*, cuticle; *Se*, resinous secretion; *Z*, elongated, ovoid, somewhat spatulate separate cells, of which there are some 20 to 60 comprising the glandular hair. *B*, A longitudinal section through a glandular hair showing the position and arrangement of the individual cells: *St*, short stalk; *Cu*, cuticle; *Se*, resinous secretion; *Cm*, wall of individual cells; *P*, granular cytoplasm. Peltate groups of unicellular (*C*) and uniseriate (*D*) non-glandular hairs. (*A*, and *B*, after Meyer; *C* and *D*, after Vogl.)

CONSTITUENTS.—A dark brownish red resin, about 80 per cent by weight of the drug, composed principally of a crystallizing principle, rottlerin; isorottlerin; two reddish yellow resins; a coloring principle; wax; a trace of volatile oil, starch, sugar, tannin, oxalic and citric acids. Total ash, about 8 per cent; acid-insoluble ash, 6 per cent.

STANDARDS.—Kamala, when dried to constant weight at 100° C., yields not less than 66 per cent of non-volatile ether-soluble extractive, and not more than 6 per cent of acid-insoluble ash.

USES AND DOSE.—Kamala is a tæniafuge and vermifuge. Average dose: humans, 8 gm.; fowl, 0.5 to 1 gm.

Elastica, Caoutchouc, or India Rubber (U. S. P. 1894 to 1916) is the prepared latex or milk juice of *Hevea braziliensis* and probably other species of *Hevea* trees indigenous to Brazil.

Incisions in the bark permit the flow of latex which is collected in small cups attached to the tree and frequently emptied. Formerly the latex was coagulated in thin layers on a paddle over open flame and became dark brownish in color. Now the rubber is precipitated from the latex by acids in water and the washed, curdy material is pressed into thin square porous sheets.

South American rubber was known to Columbus (second voyage). Its use spread widely after MacIntosh prepared waterproof cloth in 1823, and Goodyear discovered vulcanizing in 1842. Several species of *Hevea* were planted commercially after 1876. Before World War II, the United States used about one-half (700,000 tons) of the annual production, which came largely from the Dutch and English East Indies.

Synthetic Rubber was very rapidly developed in Germany and in the United States after the Japanese shut off the supply of natural rubber. Butadiene 1, 3-CH_2:CH.CH:CH_2, a petroleum hydrocarbon, also producible from alcohol and organic waste, when polymerized with styrene (C_6H_5CH:CH_2) from storax, but synthesized commercially from ethylbenzene, forms Buna S; if the polymerization be with acrylonitrile, CH_2:CH (CN) the product is known as Buna N. Neoprene, formed by the polymerization of *b*-chloroprene, CH_2:CH.C(Cl):CH_2 derived from acetylene, contains 40 per cent of chlorine; it is superior to natural rubber as regards resistance to the action of light, ozone, and organic solvents. Many other types of synthetic rubbers are known and may be produced commercially.

Caoutchouc is insoluble in water, dilute acids, or dilute solutions of the alkalis; more or less soluble in chloroform, carbon disulfide, oil of turpentine, benzine and benzol. It melts at about 125° C., remaining soft and adhesive after cooling.

India Rubber consists chiefly of two hydrocarbons, one of which is ductile and readily soluble in chloroform, and the other elastic and less soluble in chloroform; it also contains 1 to 2 per cent of resin and volatile oil.

India Rubber retains its elastic and other properties and is not affected by heat, if it is first purified and then mixed with sulfur or sulfides. Ordinary rubber articles are prepared in this manner. Hard-rubber articles are manufactured from Borneo rubber, to which colophony, gum balata and caoutchouc are added, a number of mineral substances being added to cheapen as well as to color the final product.

Elastica is used pharmaceutically as a basis for plasters and in the manufacture of many surgical implements, syringes and catheters. It has no therapeutic action.

ALLIED PRODUCTS.—**African rubber** is obtained from several species of *Landolphia* and *Kickxia elastica* (Fam. *Apocynaceæ*). **Bahia rubber** is derived from *Hancornia speciosa* (Fam. *Apocynaceæ*). **Central American** or **Panama rubber** is obtained from *Castilloa elastica* (Fam. *Moraceæ*). **Ceara rubber** is the product of *Manihot glaziovii* (Fam. *Euphorbiaceæ*). **East India rubber** is the product of the commonly cultivated rubber plant, *Ficus elastica* (Fam. *Moraceæ*). **Guayule rubber** from *Parthenium argentatum* Gray, was extensively produced in southern California and northern Mexico during World War II. **Penang** or **Borneo rubber** is the product of several species of *Urceola* (Fam. *Apocynaceæ*).

Cascarilla Bark (U. S. P. 1820 to 1905; N. F. 1916 to 1926) is the dried bark of *Croton eluteria*, a tree-like shrub indigenous to the West Indies. The commercial supplies are chiefly obtained from Nassau, Bahama Islands. The bark is now used to a limited extent in medicine. On account of the aromatic odor which it emits on burning, it is used in fumigating mixtures. It is largely used in flavoring liquors and in scenting tobacco. It occurs in quills or transversely curved pieces, 4 to 12 mm. in width, and 0.2 to 3 mm. in thickness; externally grayish brown with patches of foliaceous lichens having minute black apothecia, longitudinally wrinkled and transversely fissured; inner surface dark brown, longitudinally striate; fracture short, uneven, resinous; fractured surface showing an easily exfoliated cork; primary cortex more or less mottled from the whitish oil cells and the brownish resin cells; secondary cortex, dark reddish brown with narrow, white medullary rays, between which are distributed the strands of leptome and secretion cells; odor aromatic, fragrant; taste aromatic and very bitter. Cascarilla contains 1 to 1.5 per cent of a volatile oil, containing eugenol, limonene, an oxygenated principle; and cascarillin, tannin and vanillin. Cascarilla is an aromatic bitter and a tonic.

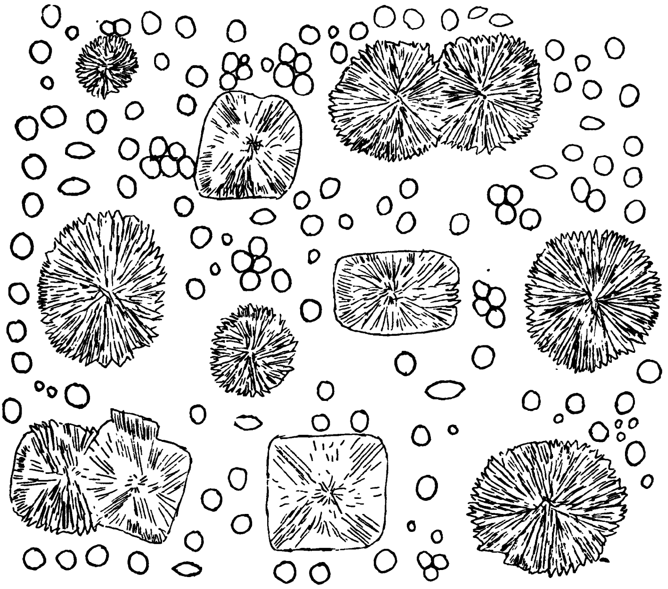


FIG. 211.—Microscopic appearance of latex in *Ficus elastica*, showing small globules and sphero-crystals which separate soon after the removal of the fresh latex. (From a drawing by Hogstad.)

Cassava Starch, Para or Brazilian Arrowroot is the starch obtained from the thickened roots of the bitter cassava (*Manihot utilissima*) and the sweet cassava (*Manihot palmata*), perennial herbs native of South America and extensively cultivated in the West Indies, tropical South America and to some extent in Florida and other southern states. The plants are very easily grown and produce very large roots, weighing sometimes 5 kg. At harvest time the roots are dug, washed, cut and scraped, whereby the starch grains are released and finally obtained by methods similar to those employed in the manufacture of potato starch. The starch is obtained in large quantities in Brazil from the root of the bitter cassava, the hydrocyanic acid being eliminated in the process of washing and drying. In Florida considerable starch is made from the sweet cassava. As this starch is sold very often at a price below even that of corn starch, it is used to some extent in the arts, chiefly as a sizing for cotton fabrics

Cassava starch occurs as a fine, mobile powder, the grains being mostly single or 2- to 8-compound, the individual grains being somewhat planoconvex or bell-shaped, varying from 5 to 30 microns in diameter and having a distinct central circular or radiating cleft (Fig. 46).

Tapioca (U. S. P. 1820 to 1882) is formed by heating the cassava starch while it still contains a maximum degree of moisture. It is heated upon iron plates, first at a low temperature, which is gradually increased until the starch grains are agglutinated into the familiar form of "pearl tapioca." Any other starch, if moistened and subjected to the same process of heating, will result in the production of forms similar to those of the genuine article. Tapioca is chiefly used in the making of puddings, and useful as a nutrient for convalescents.

ANACARDIACEÆ, OR SUMAC FAMILY

This family consists of about 400 species of trees or shrubs, sometimes climbing and very abundant in the tropics and subtropics, a few being found in the temperate zones. The typical genus, *Rhus,* of which there are a number of species found in the United States, is characterized by compound leaves, small greenish white or yellow flowers, occurring in terminal panicles, and drupaceous, often crimson-colored fruits. All of the plants of this family possess resin canals, which are situated in the phloem portion of the vascular bundle of the axis and leaves. In some few cases these are also found in the medullary rays, pith and cortex. In addition, tannin sacs occur more or less abundantly and occasionally lysigenous mucilage cavities are present. More or less crescent-shaped groups of bast fibers occur in the pericycle, enclosing on the concave side, a large resin canal; occasionally the pericycle is a composite and continuous ring of sclerenchyma. The non-glandular hairs are mostly unicellular. Glandular hairs of a number of specific forms are developed.

MASTIC

Mastic or Mastich (U. S. P. 1863 to 1916; N. F. 1916 to date) is the concrete exudation from *Pistacia Lentiscus* Linné. Mastic is from the Greek, meaning to chew; *Pistachia* is from the Persian *pistah,* the name of the pistachio tree; *lentiscus* refers to the lenticular cavities into which the resin is secreted. The plant is a shrub or small tree indigenous to the Mediterranean region, and cultivated in the Grecian Archipelago, especially on the Island of Scio. The resinous juice collects in cavities in the inner bark. Long incisions are made in the trunk and larger branches through which the resin exudes and finally collects in small tears on the outside. The origin of the use of mastic is lost in antiquity. Both Theophrastus and Pliny mention it. Mastic has long been chewed by Oriental women as a breath sweetener and even today is a common article in the Oriental bazaars. Its employment in medicine dates back to about the thirteenth century.

Description.—Somewhat globular or ovoid tears, 3 to 7 mm. in length, *moderate yellow to pale greenish yellow,* translucent, having a glass-like luster, comparatively free from *a whitish dust; brittle; fracture conchoidal, becoming* plastic when chewed; odor slight, balsamic; taste mild, terebinthinate.

The acid number is not less than 50.

CONSTITUENTS.—About 90 per cent of a resin, consisting of α-resin (mastichic acid), which is soluble in alcohol, and β-resin (masticin), which is insoluble in alcohol; a volatile oil, 1 to 2.5 per cent, with the balsamic odor of the drug and consisting chiefly of *d*-pinene. A small quantity of a bitter principle, which is soluble in hot water and is precipitated by tannin, is also present. Total ash, about 0.35 per cent; acid-insoluble ash, about 0.1 per cent.

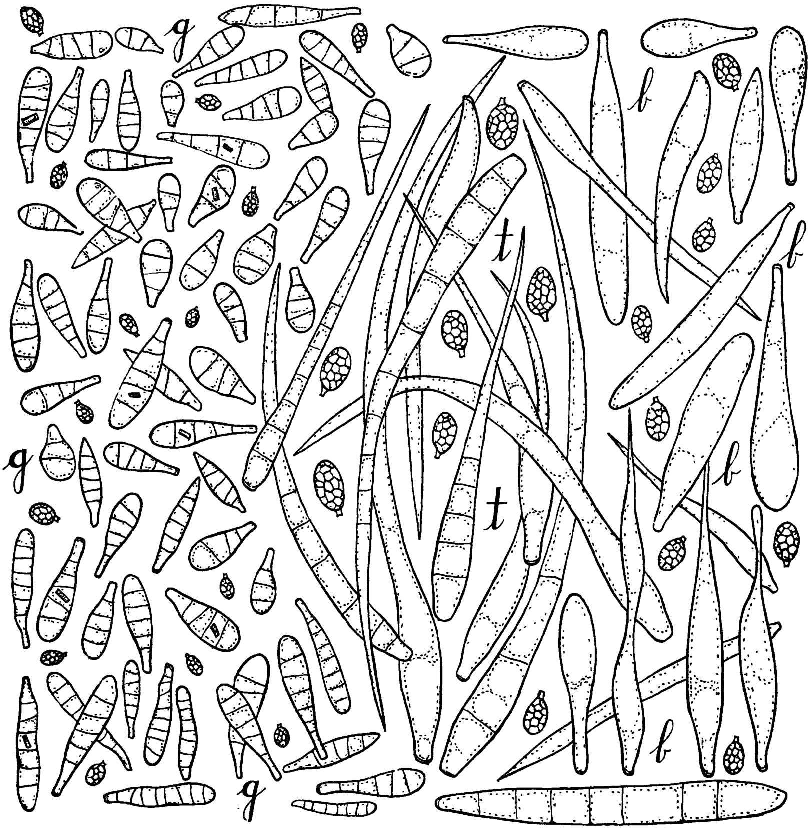


FIG. 212.—Mostly non-glandular hairs and a few of the small glandular hairs covering the surface of the fruits of several species of *Rhus*: *g*, hairs on *Rhus glabra*, being more or less broadly top-shaped or carrot-shaped to spatulate and occasionally narrow, elliptical and from 0.1 to 0.4 mm. in length; *t*, hairs on *Rhus typhina*, being long and needle-like, varying from 0.75 to 1.5 mm. in length; *b*, hairs of *Rhus glabra borealis*, being intermediate between those of *Rhus glabra* and *Rhus typhina*, varying from elongate spatulate and narrow cylindrical to needle-shaped, and from 0.1 to 1 mm. in length.

STANDARDS.—Mastic yields not more than 3 per cent of ether-insoluble residue and not more than 20 per cent of alcohol-insoluble residue. It contains not more than 1 per cent of foreign organic matter and yields not more than 0.25 per cent of acid-insoluble ash.

USES AND DOSE.—Mastic is a mild stimulant; in solution it is a protective.

Various other species of *Pistacia* found in India and northern Africa yield resins resembling mastic. **American Mastic** is obtained from the Peruvian Peppertree (*Schinus molle*). Similar resins are found in other genera of the *Anacardiaceæ*, as *Astronium* and *Semecarpus*.

Chios Turpentine is a product resembling mastic and is obtained from *Pistacia terebinthinus.* It consists of 10 to 12 per cent of a volatile oil (consisting chiefly of pinene) and 80 to 90 per cent of resin.

Rhus Glabra or Sumac Berries (U. S. P. 1820 to 1916, 1926 to 1936; N. F. 1916 to 1926) is the fruit of *Rhus glabra,* a smooth glaucous shrub, indigenous to Canada and the United States, extending as far west as Arizona. The dry drupe is superior, nearly globular, flattened, 3 to 5.5 mm. in diameter, 2.5 mm. in thickness, and with a slender peduncle about 2 mm. in length; reddish externally, very pubescent; endocarp smooth, shiny, light red; 1-locular, 1-seeded; inodorous; taste acidulous and astringent. The glandular and non-glandular hairs which are the characteristic structural elements are illustrated in Figure 212.

Rhus Glabra contains tannic acid about 2 per cent; gallic acid; and acid calcium and potassium malates. The acidity in the fruits, in terms of malic acid, varies from 6.5 to 8 per cent. Total ash about 2.79 per cent; acid-insoluble ash 0.7 per cent. It is an astringent and a tonic.

The **fruits** of the staghorn sumac, *Rhus typhina,* a shrub very abundant in the eastern United States, have replaced to some extent those of *Rhus glabra.* The drupes of these two plants closely resemble each other both in form and size, but the latter are distinguished by being covered with long, nearly straight, needle-like, crimson hairs. These hairs are frequently over 1 mm. in length, more or less undulate in outline and have relatively thicker walls. The total acidity, in terms of malic acid, ranges up to 11.22 per cent, being much higher than in Rhus Glabra.

The leaves of *Rhus glabra* contain from 16 to 25 per cent of tannin. The **galls** formed on the petioles and leaves resemble the Chinese or Japanese galls and contain about 60 per cent of tannin and some gallic acid.

Rhus Toxicodendron, Poison Ivy or Poison Oak (U. S. P. 1820 to 1905) is the fresh leaflets of *Rhus toxicodendron* (*Rhus radicans*), a woody vine common throughout the United States. It either trails over the ground or climbs by means of aerial roots or remains shrub-like. The leaves are 3-foliate, the leaflets being ovate, acuminate, nearly entire, inequilateral, 3 to 20 cm. long and with short stalks; inodorous; slightly astringent, saline and acrid in taste. The flowers are green and in loose axillary panicles. The fruit is a globular, glabrous, grayish drupe.

The poisonous constituent has been thought to be a volatile principle, or a resin emulsified in the latex, or a protein producing an anaphylactic reaction in certain humans. A phenolic oily resin, named **toxicodendrol,** and present in all of the poisonous *Rhus* species, has been proven to be the active constituent. It is not volatile; it is soluble in alcohol and in oils; it is non-nitrogenous, has phenolic groups, gives a blue green reaction with iron, and absorbs bromine readily. It is precipitated by lead acetate solution; and is gradually oxidized by exposure to air, losing its activity; the same reaction occurs rapidly with the alkali hydroxides, and, so delicate is this reaction that minute amounts of the substance may be detected by means of the microscope if the plant tissues are mounted in an alcoholic solution of potassium hydroxide.

Toxicodendrol occurs in the sticky sap of the plant, which exudes when the plant is injured; it causes dermatitis upon penetration of the epidermis of the skin. It may be conveyed by the hands or clothing from one person to another. It is not infective and apparently does not enter the blood stream, but minute quantities of it (0.001 mg.) on the epidermis may cause dermatitis. Probably persons differ in sensitiveness to the poison. Desensitization by intramuscular injection of acetone extracts of poison ivy leaves appears to confer protection against the dermatitis, and to shorten the course and mitigate the symptoms of the dermatitis already developed.

Dried poison ivy leaves are of questionable medicinal value. The drug is said to possess narcotic and antirheumatic powers.

Rhus vernix, commonly known as **Poison Sumac, Poison Elder or Poison Dogwood,** is poisonous, like *Rhus toxicodendron,* and contains the same principles. It is a shrub or small tree, found in swamps in the United States and Canada. The leaves are 7- to 13-foliate, with obovate or oval, acuminate, entire leaflets; the flowers are small, green, and in axillary panicles; the fruit resembles that of *Rhus toxicodendron*.

Other species of *Rhus* are also poisonous, as the western poison oak (*R. diversiloba*) of the Pacific Coast, and the **Japanese Lacquer** or Varnish tree (*R. vernicifera* and *R. succedanea*). The lacquer trees grow wild in both China and Japan, where they are also cultivated. The specific name *vernix* means "varnish." The lac is obtained by incising the bark and removing it with a pointed spatula. The grayish white emulsion, which contains toxicodendrol, is strained and on exposure to air it changes to brown, becoming finally black. This change is due to the oxidizing enzyme, laccase. When Japanese lac is thinned with camphor, or mixed with linseed oil, on drying in a moist atmosphere, it forms the most indestructible varnish known. Various pigments are used, as vermilion, gamboge, acetate of iron and other substances. The best glossy black colors are obtained by the addition of iron.

The tree, *Lithræa caustica*, found in Chile, causes an inflammation of the skin like that caused by *Rhus toxicodendron*. The plant contains a resin and a volatile oil. The poisonous properties are ascribed to a volatile substance resembling cardol.

Rhus semilata produces **Chinese Galls**, excrescences formed as a result of the stings of an aphis. **Japanese Galls** are similar formations occurring on *Rhus japonica*.

Anacardium.—**West Indian Cashew** is the fruit of *Anacardium occidentale*, a tree indigenous to the West Indies and extensively cultivated in the tropics. The fruit consists of a fleshy, pear-shaped receptacle having at its summit the kidney-shaped, drupaceous nut; the latter is about 3.5 cm. in length, 2 cm. in breadth and in thickness; of a very dark brown color, nearly smooth; easily cut; pericarp about 4 mm. in thickness, containing large ellipsoidal balsam canals; the seed is reniform, having a thick reddish brown seed coat and enclosing a large embryo. Anacardium contains cardol, a yellowish or reddish, oily, vesicating substance, becoming darker on exposure to the air, insoluble in water, soluble in alcohol, ether, chloroform, solutions of the alkalis and sulfuric acid, the latter solution becoming colored red; also anacardic acid, and tannic acid. The seeds contain from 40 to 50 per cent of a fixed oil, consisting mostly of glycerides of oleic acid with some stearic acid and cholesterin. Anacardium has been used as a vesicant and as an escharotic. It also is said to be a vermifuge. The oil is administered as a vermifuge in an average dose of 0.2 gm. The kernel, raw or roasted, is edible. The fleshy receptacle of the West Indian cashew after maturing is sweet and edible. In Brazil, a wine, said to resemble Madeira wine, is made from it.

Oriental Cashew-nut is the fruit of *Semecarpus anacardium*, a tree indigenous to northwestern India and widely distributed in southern Asia. The fruits resemble those of the West Indian cashew-nut and contain similar principles, viz., cardol, anacardic acid and tannic acid. They also contain an alkaloid, chuchunine, which resembles strychnine in its action.

The resinous juice of the stem furnishes a varnish; and the fixed oil from the seeds is used in India for a floor dressing, to protect from the attacks of white ants.

Pistachio Nut, or Green Almond, is the seed of *Pistacia vera*, a tree indigenous to western Asia and cultivated in the Mediterranean countries and also in California. These seeds are extensively used in confectionery and are from 10 to 25 mm. in length, somewhat quadrangular in cross-section and consist of two fleshy green cotyledons. They are readily determined by the carmine or brown coloring matter in the seed coat, which becomes green upon the addition of solutions of alkalis, and by the exceedingly small polygonal cells with porous walls of the inner epidermal layer of the seed coat. Almond and other seeds dyed with coal-tar colors are sometimes substituted for the genuine article.

Prinos or Black Alder (U. S. P. 1820 to 1894) is the bark of *Prinos verticillatus* Linné (*Ilex verticillata* Gray) (Fam. *Aquifoliaceæ*).

This black alder or winterberry is a shrub 2 to 3 meters high, growing in swampy ground in Canada and northern United States. The bark is thin, in slender pieces, or in fragments, brownish with light-colored lichens with dark apothecia. It is inodorous, with a bitter astringent taste. It contains tannin and an amorphous bitter principle. It has been used as an astringent, tonic and alterative. Dose, 2 gm.

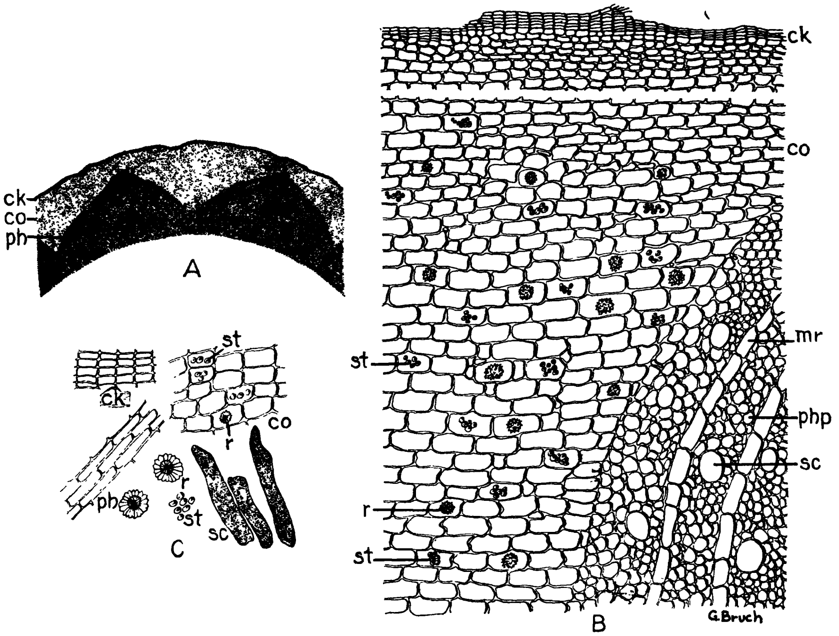


FIG. 213.—Euonymus: *A*, lens view of the bark in transverse section: *ck*, thin layer of cork; *co*, broad cortex, penetrated by broad wedges of phloem (*ph*). *B*, Transverse section of outer portion of bark: *ck*, cork of small cells with thin, nearly colorless lignified walls; *co*, cortex of tangentially elongated parenchyma, bearing starch and calcium oxalate rosettes; a portion of the phloem area showing curved, 1-cell wide medullary rays (*mr*), sieve strands and phloem parenchyma (*php*), and secretory cells (*sc*). *C*, Elements of the powder: cork fragments (*ck*); fragments of parenchyma from the cortex (*co*) and phloem (*ph*); calcium oxalate rosettes (*r*), mostly about 30 microns in diameter; starch (*st*) nearly spherical and up to 21 microns in diameter; elongated, yellowish to brownish amorphous masses of caoutchouc latex (*sc*) or latex cells. (Drawings by G. Bruch.)

CELASTRACEÆ, OR STAFF TREE FAMILY

The plants are trees, shrubs or woody climbers, represented by about 45 genera and 450 species, which are widely distributed. The leaves are simple, the flowers are small and regular, the fruit is a somewhat fleshy dehiscent pod, and the seeds usually have a reddish or purplish aril. The plants are furthermore distinguished by the development of caoutchouc-containing elements in the phloem. These resemble laticiferous tubes, having narrow lumina and caoutchouc-like contents, which are soluble in chloroform, ether and similar solvents. They are frequently so abundant, as in *Euonymus*, that when the bark is broken the fragments remain connected by the tough elastic threads. The cork-wings, which are peculiar to a number of species of *Euonymus,* are due to the development of cork in the parenchyma of the cortex. This usually arises at four different points, thus elevating the epidermis and giving the branches a 4-angled or slightly winged character.

Euonymus or Wahoo Bark (U. S. P. 1863 to 1916; N. F. 1916 to 1947) is the dried bark of the root of *Euonymus atropurpureus* Jacquin. *Euonymus* is from the Greek meaning "good name;" the common name of the plant "Spindle Tree," well describes the form of growth; *atropurpureus* means "dark purple," in reference to the color of the stems. The plant is an erect shrub or slender tree growing in the eastern and central United States and Canada. The Indians introduced the drug to the early settlers; it is described in the early American works on domestic medicine.

The drug occurs in transversely curved pieces or single quills, the bark 0.5 to 4 mm. in thickness; very light in specific gravity; outer surface light brown, with scaly patches of soft gray cork, few lenticels and root scars; adhering roots frequently perforate the bark; inner surface light gray, longitudinally striate, somewhat porous; fracture short, with silky, projecting caoutchouc strings; cork light brown; inner and middle bark somewhat tangentially striate and with irregular, dark brown bast areas; odor faint; taste bitter and acrid.

The stem-bark occurs in very long, fibrous strips with a grayish black cork and should be rejected.

Structure and Powder.—See Figure 213.

The drug contains volatile oil, 1.3 per cent; a phytosterol glucoside; dulcitol; starch; tannin; a mixture of fatty acids; furan-α-carboxylic acid; euonymol, euonysterol, and atropurol. Total ash, about 8.75 per cent; acid-insoluble ash, about 2 per cent.

Euonymus is a mild purgative. It has a mild effect upon the heart, similar to that of digitalis. Average dose, 0.5 gm.

Adulterants.—The bark of Wafer Ash (*Ptelea trifoliata*) is occasionally substituted. It occurs in quills or transversely curved pieces from 3 to 4 mm. in thickness; outer surface light brown with transverse ridges and grayish white lenticels; fracture short; broken surface pale yellow and waxy.

Allied Drugs.—*E. europæus* and other species of *Euonymus* are also used in medicine and probably contain the same constituents.

ACERACEÆ, OR MAPLE FAMILY

This family consists of shrubs or trees, represented chiefly by the genus *Acer,* of which there are about 100 species, growing abundantly in the United States, Canada, China and Japan. They are extensively used as shade trees and a great many horticultural varieties have been produced, those of Japan being known for their highly dissected leaves and their brilliant colorings. The wood of the maple is extensively employed in the manufacture of furniture and flooring and for a variety of purposes. The sap of the Sugar or Rock Maple (*Acer saccharum*) is the chief source of **Maple Sugar.** It is produced in New England, especially Vermont but also in New York, Ohio, Indiana, Michigan, etc.

The trees are "tapped" in early spring when the sap begins to rise; it is collected through spiles driven into the sap wood, evaporated in kettles over open fires and enters market as syrup or loaf sugar. The unrefined products are much more tasty than the refined sugar. The yield per tree is 3 to 6 pounds of sugar annually, and a "sugar grove" may be worked for many years without harm to the trees. A small amount of sugar is also obtained from the Black Sugar Maple (*Acer saccharum nigrum*) and the Silver or White Maple (*Acer saccharinum*). The family yields no drugs but the reader is referred to Viburnum Opulus under which the Mountain Maple (*Acer spicatum*) is discussed as an adulterant.

SAPINDACEÆ, OR SOAPBERRY FAMILY

This is a large family of over 1000 species, chiefly tropical woody climbers. They are especially characterized by the presence of glucosidal saponins which have the property of frothing with water, so that some of them have been employed as substitutes for soap, as the fruits of *Sapindus*, a tree widely distributed from Arizona to northern Mexico. Several forms of secretory cells are also found in this family, one being more or less spheroidal or irregular in shape and another in the form of elongated tubular cells, frequently arranged in uniseriate rows. The contents vary from yellowish brown to brownish black and apparently contain saponin. Some of the secretion cells give a reaction with ferric salts for tannin. The walls of the epidermal cells are frequently modified to mucilage, and the cells on the dorsal surface may be papillose. Glandular and non-glandular hairs occur in a number of specific forms.

Guarana (U. S. P. 1882 to 1926; N. F. 1926 to 1947) is a dried paste consisting chiefly of the crushed seed of *Paullinia cupana* Kunth. The plant is a climbing shrub native to Brazil and Uruguay. The seeds are collected by the Indians, roasted over fires for about half a day; the kernels ground to a pasty mass with water in crude stone mortars; the paste molded into cylindrical sticks which are dried in the sun or over fires.

Guarana is used in the preparation of a beverage which is used like tea and coffee by the people of Brazil. Guarana was introduced into France from South America in 1817 and caffeine was discovered as its principal constituent in 1840. The original discovery by the Indian tribes is lost to record.

The drug is in cylindrical sticks up to 30 cm. in length, and 50 mm. in diameter; externally blackish brown, surface marked by depressions, but otherwise smooth; hard, heavy and brittle, the fracture being uneven; internally light brown to reddish brown, somewhat variegated from the fragments of contused seeds.

The powder is light pinkish brown; odor slight; taste astringent, bitter; consisting mostly of irregular masses of parenchyma cells, containing more or less altered starch grains; unaltered starch grains, from 10 to 25 microns in diameter, spheroidal, ellipsoidal, broadly ovoid or polygonal in shape; occasionally narrow, elongated, sclerenchymatous cells, with thick, yellowish and non-lignified walls are noted.

The drug contains caffeine, 2.5 to 5 per cent; tannin (catechu-tannic acid), about 25 per cent; considerable starch; a small amount of catechin; a volatile oil; an acrid, green fixed oil; and saponin. Total ash, about 1.6 per cent; acid-insoluble ash, 0.15 per cent.

Guarana yields not less than 4 per cent of anhydrous caffeine and not more than 0.5 per cent of acid-insoluble ash. Place a drop of hydrochloric acid on a slide, add to it about 1 mg. of powdered guarana and one drop of gold chloride T.S., allow the mixture to stand for a few minutes, and crystals of caffeine gold chloride should separate in the form of orthorhombic plates or in needles, the latter usually in spheroidal aggregates (see page 433) Microcrystals of caffeine may be obtained upon microsubliming powdered guarana.

Guarana is a nervine and a stimulant, its action being due to the caffeine that is present. It is also an astringent and a tonic. Average dose, 2 gm.

RHAMNACEÆ, OR BUCKTHORN FAMILY

This is a family of 45 genera and over 500 species, consisting of shrubs or trees, often woody climbers, and rather widely distributed. The leaves are mostly simple and stipulate, the flowers are small and regular and the fruit is a drupe or capsule. The twigs of some of the species, as *Rhamnus cathartica,* possess stout thorns, hence the name buckthorn as applied to this species and the family. Many of the plants are characterized by the presence of methyl-anthraquinone derivatives, which give a bright red color with solutions of the alkalis. These derivatives are found in the medullary rays and distributed among the parenchyma

FIG. 214.—Peeling cascara bark in Washington forests. Illustrating a method employed in commercial collection and the dense forest in which the collector must work. (After Johnson and Hindman.)

cells of the cortex. Plants of this family may contain idioblasts having brown contents, or secretory cavities containing a brown amorphous substance, or mucilage cavities. The latter when present are distributed in the parenchyma of the cortex and in the veins of the leaves. The walls of the epidermal cells sometimes are modified to mucilage. The leaf-teeth are differentiated into glands and the non-glandular hairs are unicellular, uniseriate or stellate. Glandular hairs do not occur.

FIG. 215.—Transporting cascara bark on pack horses to wagon road. (After Johnson and Hindman.)

CASCARA SAGRADA

Cascara Sagrada (U. S. P. 1894 to date) is the dried bark of *Rhamnus purshiana* DeCandolle. It should be kept dry for at least one year before being used in medicinal preparations. The name *Cascara Sagrada* is Spanish for sacred bark; *Rhamnus* is the ancient classical name for buckthorn; *purshiana* was given in honor of the German botanist, Fred Pursh. The plant is a tree attaining the height of 20 meters, indigenous to the Pacific Coast of North America. Most of the present-day market supply comes from Oregon, Washington and southern British Columbia. Collections are made during the spring and summer. The wild trees are scattered in the native forests on the mountains and collectors usually operate on foot and horseback. The bark is stripped from the tree by making longitudinal incisions about 4 inches apart and peeling off sections which tend to roll into large quills. The trees are often felled and the bark also removed from the larger branches. The bark is sacked and conveyed on horseback and truck to suitable places, often saw mill platforms, for sun-drying. After the large quills are dried they are run through a "breaker" and broken into small transversely curved pieces which are packed in bags. Due to the possible depletion of the trees, projects for the cultivation of cascara are under way in Oregon, Washington and in British Columbia.

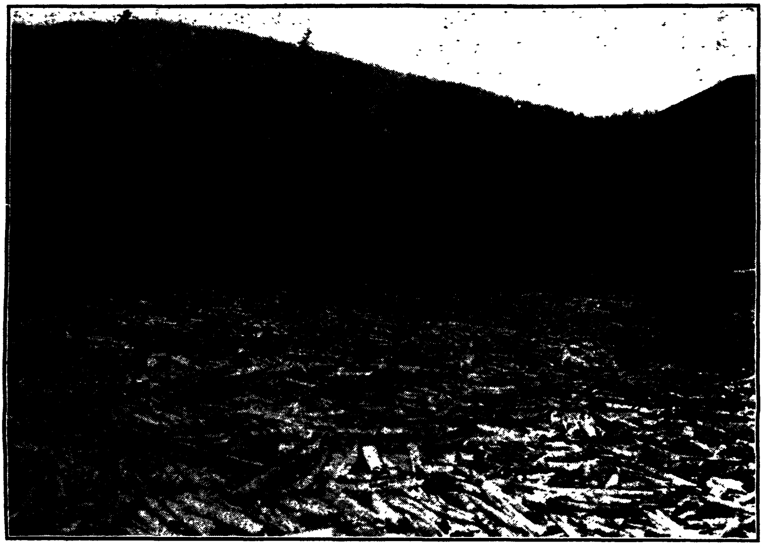


Fig. 216.—Sun-drying cascara bark on platform of abandoned saw-mill. (After Johnson and Hindman.)

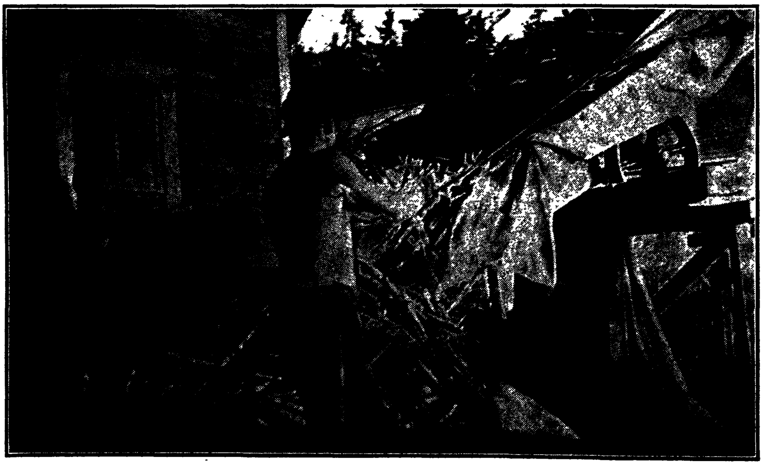


Fig. 217.—A means of moving dried cascara bark to bark cutter. (After Johnson and Hindman.)

According to tradition, cascara bark (probably *Rhamnus californica*) was known to the early Spanish priests of California. It was introduced

FIG. 218.—Cutting and sacking dried cascara bark. (After Johnson and Hindman.)

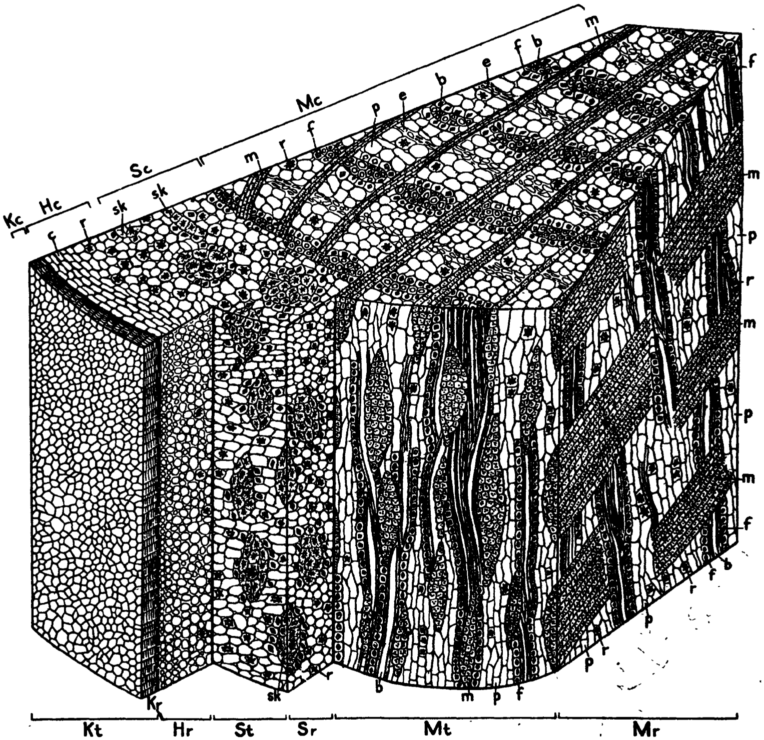


FIG. 219.—Rhamnus Purshiana in transverse (*Mc*), radial-longitudinal (*Mr*) and tangential-longitudinal (*Mt*) sections: *Kc*, *Kr* and *Kt*, transverse, radial and tangential sections of the cork, consisting of several layers of small rectilinear, thin-walled, yellowish brown to reddish brown cork cells; *Hc* and *Hr*, transverse and radial sections of the collenchymatous (*c*) outer layer of the cortex; *Sc*, *Sr* and *St*, the respective sections of the inner cortex, showing large groups of stone cells (*sk*) and parenchyma with crystals of calcium oxalate; *Mc*, *Mr* and *Mt*, the respective sections of the inner bark showing the medullary rays (*m*), up to 4 cells in width and 15 to 25 cells in height, bast fibers (*b*) in tangential elongated groups, the walls of the fibers thickened and lignified, crystal fibers (*f*) surrounding the bast bundles, sieve (*e*) in narrow strands, and parenchyma (*p*) with starch or calcium oxalate contents. (After Kraemer.)

into medicine in 1877 by Dr. J. H. Bundy after which it rapidly became a favorite, and today is in demand all over the world.

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 218, 219, 220 and the U. S. Pharacopœia.

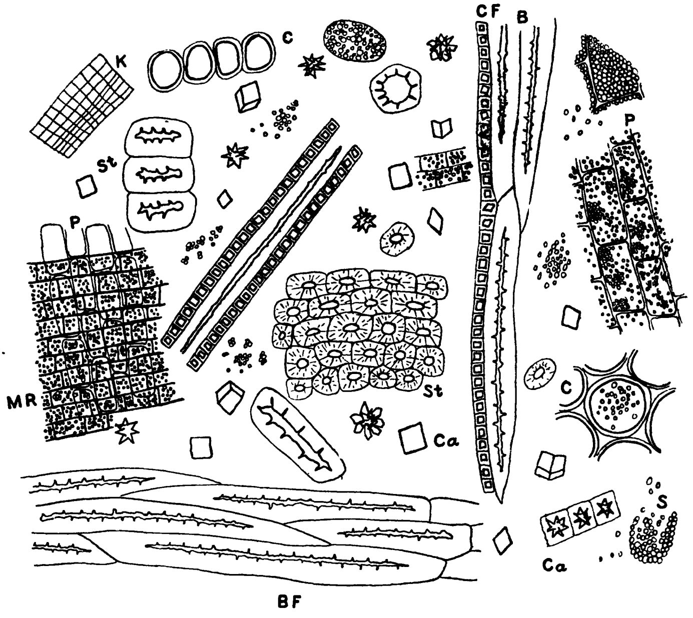


FIG. 220.—Powdered Cascara Sagrada. Light brown to olive brown; consisting largely of groups of bast fibers (*B*) with their associated crystal fibers (*CF*), the latter especially prominent in phloroglucin T.S. or chloral T.S. mounts; almost equally numerous are the groups of stone cells (*St*) which are frequently associated with parenchyma containing large rhombohedra of calcium oxalate (*Ca*); fragments of parenchyma and medullary ray cells colored red upon the addition of solutions of the alkalis; starch grains (*S*) either free or in parenchyma cells, the individual grains somewhat spheroidal, from 3 microns to 8 microns in diameter; calcium oxalate (*Ca*) in monoclinic prisms or rosettes from 6 microns to 20 microns in diameter, occasionally up to 45 microns; occasional fragments of yellowish or reddish brown cork (*K*).

CONSTITUENTS —George D. Beal and co-workers in a series of reports (A. Ph. A. J., 1922 to 1942) have presented much light upon this difficult subject:

Upon hydrolysis of the constituent cascara glycosides rhamnose and dextrose are found in the approximate ratio of 1:1, and the rate of hydrolysis indicates that these sugars are present in true glycosidic linkage. Among the aglycones obtained from cascara are:

Emodin or frangula-emodin, 4, 5, 7-trihydroxy-methyl-anthraquinone.
Iso-emodin, 3, 5, 8-trihydroxy-methyl-anthraquinone.
?-emodin, 1, 6, 8-trihydroxy-2-methyl-anthraquinone.
Aloe-emodin, 1, 8-dihydroxy-anthraquinone-3-carbinol.
Methylhydrocotoin, 2, 4, 6-trimethoxy-benzophenone.
Chrysophanic acid, 4, 5-dihydroxy-2-methyl-anthraquinone.

The total anthraquinones found in cascara sagrada was 3.81 per cent and 1.11 per cent were in the free state. Dialysis is the most expedient method of separating the inert material from the active ingredients of the fluidextract of cascara. The activity of the fluidextract was not altered appreciably by: (*a*) complete hydrolysis of the glycosides present, or (*b*) by extraction of the free anthraquinones.

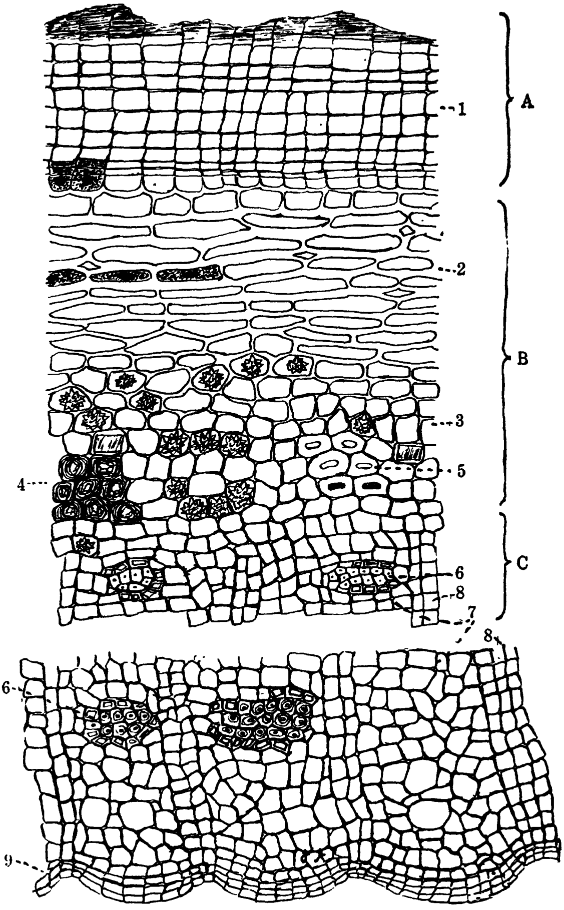


FIG. 221.—Transverse section of the bark from a ten-year-old stem of *Rhamnus californica: A*, Outer bark; *B*, middle bark; *C*, inner bark. 1, Cork, the outermost rows compressed; 2, collenchyma, strongly elongated tangentially with much-thickened walls; 3, parenchyma with numerous rosettes and prisms of calcium oxalate; 4, group of stone cells; 5, unlignified primary bast; 6, lignified secondary bast with crystal fibers; 7, phloem parenchyma; 8, medullary ray; 9, the cambium, the edge showing the waviness characteristic of this bark. (Drawing by E. N. Gathercoal.)

A mixture of 10 mg. each of aloe-emodin and emodin plus 5 mg. of chrysophanic acid was distinctly more active on guinea pigs than 25 mg. of any one of the three components tested separately. The supplementary or synergistic action observed for the mixtures of active ingredients appears to provide an explanation of the marked activity of crude extracts of cascara compared with the relatively poor activity of any of the purified fractions thus far studied.

The bark also contains rhamnol arachidate, a fat; a bitter principle; several resins; tannin; glucose; starch; calcium oxalate. Total ash, about 5.2 per cent; acid-insoluble ash, about 0.15 per cent.

Cascara bark contains from 0.0137 to 0.0223 per cent of manganese. Many other laxative drugs contain manganese, and Westman and Rowat have suggested the establishment of a manganese number for the valuation of the extracts of this class of drugs.

STANDARDS AND TESTS.—Cascara contains not more than 4 per cent of foreign organic matter. It should be collected at least one year before being used for making medicinal preparations. Cascara gives a red color when treated with ammonia T.S. If 0.1 gm. of powdered cascara is boiled with 10 cc. of water, cooled, filtered, the volume of the filtrate made up to 10 cc. and 10 cc. of ammonia T.S. added, an orange-yellow color is produced in the mixture. Cascara Sagrada produces a yellowish red color with the modified Bornträger test as given in the Pharmacopœia.

USES AND DOSE.—Cascara Sagrada is a tonic laxative. Its bitterness also makes it somewhat stomachic. Its principal use is in the correction of habitual constipation where it not only acts as a laxative but restores natural tone to the colon. The bitter taste and the activity is considerably reduced by treating cascara sagrada extracts with alkaline earths or magnesium oxide. Average dose, 1 gm.

Cascara Sagrada from *Rhamnus californica*, a shrub indigenous to southern California and the neighboring states, yields a bark which closely resembles that of *Rhamnus purshiana*, but may be distinguished by the following characters: uniformly covered with grayish lichens having numerous black apothecia; the inner surface is light or dark brown, smooth and finely striate; the collenchymatous cells are larger and the walls somewhat thicker; the medullary rays extend in more or less parallel, wavy rows and are from 1 to 7 cells in width and from 10 to 30 cells in height; the cambium margin is distinctly crenate or undulate, as the tissues shrink inward at each of the medullary rays; nearly all of the cells, with the exception of the lignified tissues, contain the oxymethylanthraquinones and are colored pinkish red upon the addition of the solutions of the alkalis.

Frangula or Buckthorn Bark (U. S. P. 1882 to 1926; N. F. 1926 to 1947) is the dried bark of *Rhamnus frangula* Linné. The specific name *frangula* means "brittle," in reference to the brittle stems of this species. The plant is a shrub attaining the height of about 5 meters growing in Europe and western Asia. The bark is stripped from the stems and branches during the spring and early summer and carefully dried. Like cascara it contains an emetic principle in the fresh condition and the bark must be aged a year or more before it is used for medicinal preparations. Most of the commercial supply comes from Germany and Russia. Decoctions of the bark have been used from an early date for cathartic purposes. It seems, however, not to have come into professional medical use until the nineteenth century.

DESCRIPTION.—In single or double quills often crushed and flattened, bark 0.3 to 1 mm. in thickness; outer surface dusky red to light olive brown, with numerous light-colored, transverse lenticels 1 to 5 mm. in length, and with grayish patches of foliaceous lichens bearing dark-colored apothecia; older bark with a brownish, roughened cork; inner surface dusky red to dusky yellowish orange with purplish blotches, smooth, longitudinally striate, and reddened by solutions of the alkalis; fracture short, with projecting bast fibers in the inner bark.

STRUCTURE.—See Figure 222.

POWDER.—Yellowish brown; odor distinctive; taste slightly bitter, astringent and acrid; bast fibers 10 to 20 microns in diameter, with very thick lignified walls and numerous pores, and usually associated with crystal fibers; calcium oxalate in rosettes or monoclinic prisms from 7 to 15 microns in diameter; starch grains nearly spheroidal, 3 to 10 microns in diameter, not numerous; parenchymatous cells with yellowish or purplish brown contents, colored red by solutions of alkalis. Stone cells are absent (distinction from cascara sagrada).

Frangula contains a glucoside, frangulin, which occurs in yellow crystals, insoluble in water and nearly so in alcohol, giving a bright purple color with solutions of the alkalis, and on hydrolysis yielding rhamnose and emodin; glucofrangulin, from the fresh bark, which hydrolyzes into frangulin and glucose during the drying of the drug; pseudofrangulin (frangulic acid), a glucoside which yields pseudo-emodin; rhamnoxanthin, a coloring principle; a volatile oil; tannin; starch; calcium oxalate. Total ash, about 4 per cent, with about 0.45 per cent of acid-insoluble ash.

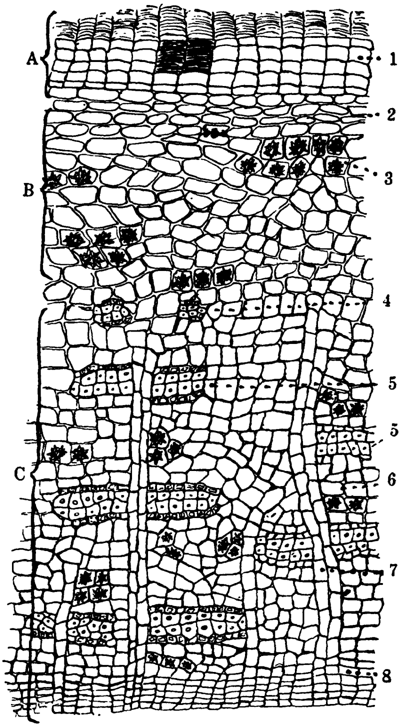


FIG. 222.—Transverse section of the bark from a nine-year-old stem of *Rhamnus frangula*: *A*, Outer bark; *B*, middle bark; *C*, inner bark. 1, Cork, the outermost rows compressed and containing a purplish black content, thus distinguishing the bark from cascara sagrada; 2, collenchyma; 3, middle bark parenchyma with numerous rosettes of calcium oxalate crystals; 4, the earliest secondary bast; 5, secondary bast of later growth with accompanying crystal fibers; 6, phloem consisting mostly of parenchyma with some rosettes of calcium oxalate; 7, medullary ray, practically free from crystals; 8, cambium. (Drawing by E. N. Gathercoal.)

When 0.1 gm. of powdered frangula is boiled with 10 cc. of water, cooled and filtered, the filtrate is colored deep red by the addition of ammonia water. Frangula produces a distinct cherry red color with the modified Bornträger's test.

Frangula is a mild laxative or cathartic. In the United States it has been largely replaced by cascara sagrada, except in veterinary practice.

The bark of *Rhamnus carniolica* has been substituted for *R. frangula*. It occurs in quills or transversely curved pieces, the bark being from 1 to 3 mm. in thickness; externally the cork is reddish brown, having numerous grayish lichens and obscure light brown lenticels from 1 to 2 mm. in width; the inner surface is grayish or dark brown and longitudinally striate; the fracture is short-fibrous; the odor slight; and the taste, bitter and astringent. The older pieces are distinguished by having a deeply fissured cork and groups of stone cells. In the younger bark the medullary rays are from 4 to 7 cells in width.

The bark of *R. cathartica* (see Fig. 223) possesses cathartic properties and has been used like frangula.

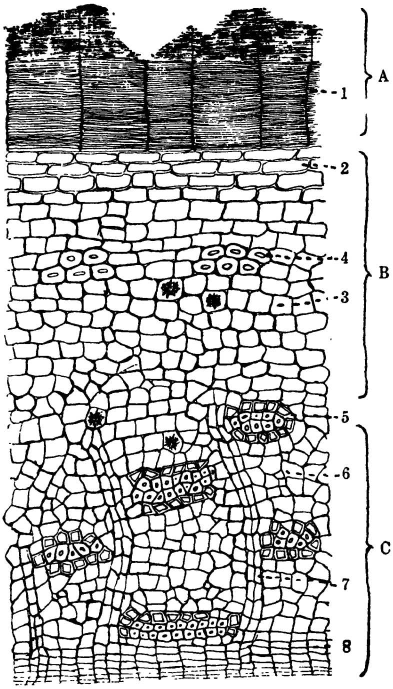


FIG. 223.—Transverse section of the bark of *Rhamnus cathartica* from a four-year-old stem. *A*, Outer bark; *B*, middle bark; *C*, inner bark. 1, Cork, many rows of narrow cells much elongated tangentially; 2, collenchyma of a few poorly differentiated rows; 3, parenchyma with some calcium oxalate rosettes; 4, unlignified primary bast; 5, lignified secondary bast with crystal fibers; 6, phloem parenchyma; 7, medullary ray; 8, cambium. (Drawing by E. N. Gathercoal.)

Rhamnus Cathartica, Buckthorn Berries, or Baccæ Spinæ Cervinæ (U. S. P. 1820 to 1831; N. F. 1916 to 1947) is the dried, ripe fruit of *Rhamnus cathartica* Linné. The specific name *cathartica* refers to the purgative properties of the drug. The plant is a thorny shrub indigenous to northern Africa and central Asia, but widely distributed in Europe and naturalized in the eastern United States. The ripe fruits are collected in the fall and enter commerce mostly from Hungary. Buckthorn fruits were known as a laxative under the name of **Waythorn** or **Hartshorn** before the Norman Conquest. The Welsh physicians of the thirteenth century prescribed a preparation of the berries under the name of Syrup of Buckthorn.

For the description and structure of the fruits and the powder see Figure 224 and the National Formulary, Seventh Edition.

Buckthorn Berries contain rhamno-emodin, apparently the most active principle; several coloring principles including: rhamnocitrin, in golden yellow crystals which on hydrolysis forms *b*-rhamnocitrin; rhamnolutin in yellow needles, and isomeric with luteolin and fisetin; rhamnochrysin in orange needles; violet anthocyanin; and chlorophyll.

Rhamnus Cathartica, when macerated in water, assumes its original globular shape, about 1 cm. in diameter. The expressed pulp is colored red by acids and greenish yellow by alkalis. If an aqueous infusion of the fruit is shaken with ether and the separated ethereal layer then shaken with diluted ammonia water, the latter becomes cherry-red.

Rhamnus Cathartica is a purgative. Average dose, 1 gm.

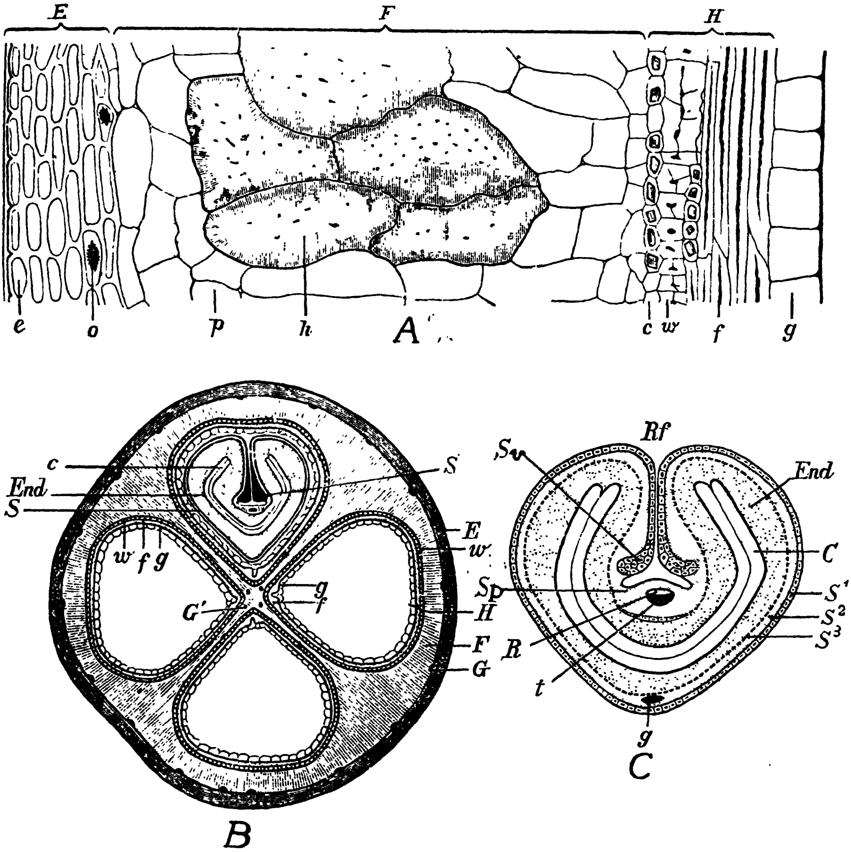


FIG. 224.—Rhamnus Cathartica: *A*, Cross-section through wall of the fruit: *E*, pericarp; *F*, sarcocarp; *H*, endocarp; *e*, epidermis; *o*, calcium oxalate in cells of hypodermis; *p*, parenchyma; *h*, secretion cells containing a substance which is insoluble in alcohol or hydrated chloral solutions, soluble in solutions of potassium hydroxide, and colored reddish brown or greenish with ferric chloride solutions; *c*, calcium oxalate cells of endocarp; *w*, sclerotic cells; *f*, sterome cells. *B*, Cross-section of entire fruit, showing one seed; *E*, *F*, *H*, *g*, *f*, *w*, as in *A*; *S*, seed coat; *S'*, outer wall of seed coat; *End*, endosperm; *c* cotyledons; *G*, vascular bundle. *C*, cross-section of a seed: S^1, S^2, S^3, different layers of the seed coat; *R*, vascular bundle of raphé; *t*, position of vessels of mestome strand; *g*, mestome strand; *Rf*, cleft in which raphé is situated; *End*, endosperm; *C*, cotyledons; *Sv*, cells with thick walls; *Sp*, parenchymatous cells. (After Meyer.)

ALLIED DRUGS.—The fruits of *Rhamnus cathartica*, as well as those of *R. infectoria* (known as **French Berries**) and of *R. saxatilis* (called **Persian Berries**) have been used as yellow dyes. The fruits of several species growing in China yield a green indigo.

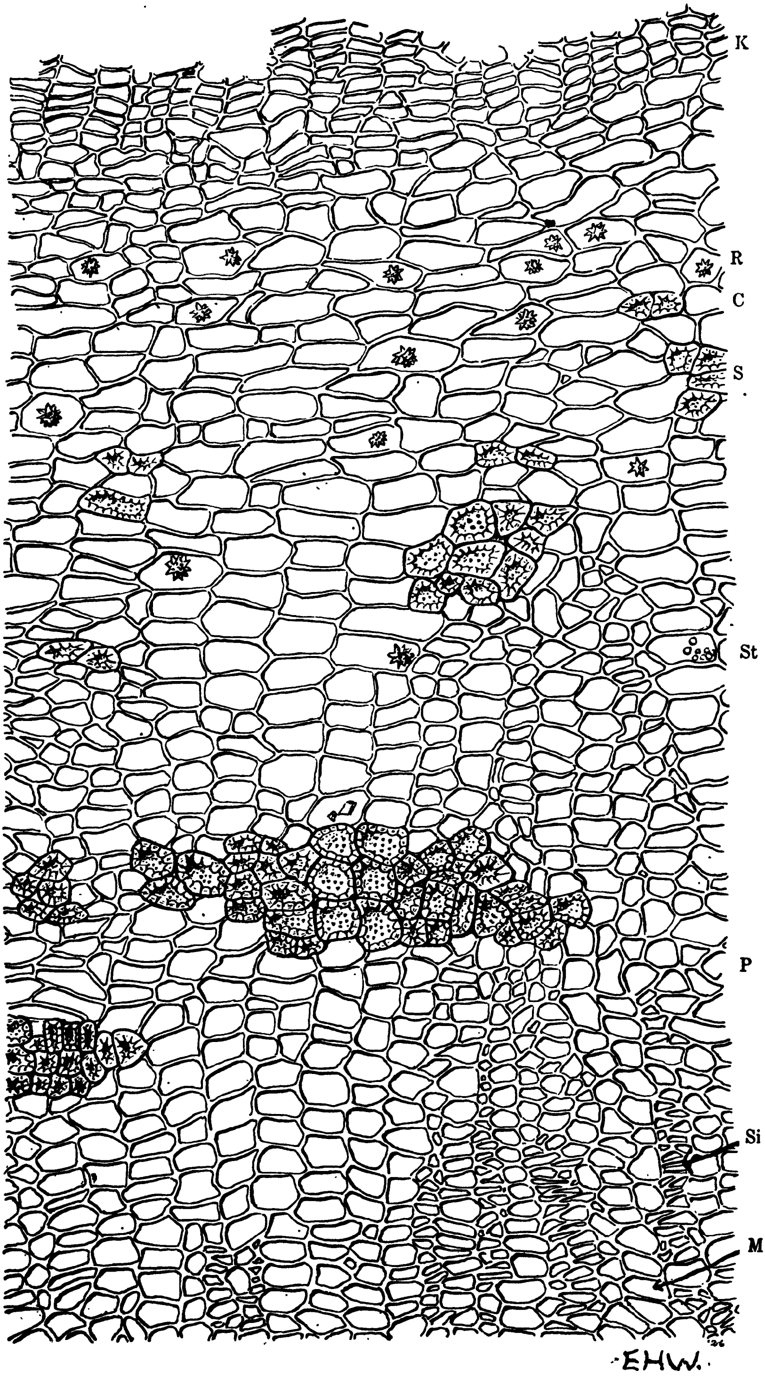


FIG. 225.—*Ceanothus americanus.*—Transverse section of root bark: *K*, cork; *C*, cortex; *P*, phloem; *R*, rosettes of calcium oxalate; *St*, starch; *S*, stone cells; *Si*, sieve; *M*, medullary rays. (Drawing by E. H. Wirth.)

Ceanothus, New Jersey Tea, or Red Root, is the dried bark of the root of *Ceanothus americanus*, a branching shrub, 6 to 12 dm. high, of the eastern and central United States and Canada. The large woody root with many branches is terminated with a knotty crown producing numerous slender stems. The plant has long been known as an astringent, and during the Revolution the dried leaves served as a substitute for tea. Recently the drug has been shown to possess marked blood-coagulative powers when administered by mouth. The bark occurs in short quills or curved pieces, 1 to 3 mm. thick; grayish to reddish brown, smooth or roughened by longitudinal furrows, inner surface usually reddish brown, striate or smooth; short, uneven granular fracture; odorless; taste astringent and bitter. The structure is shown in Figure 225.

Ceanothus contains tannin 10 per cent, phlobaphenes, resin, oil, and a mixture of alkaloids, one of which has been crystallized. Total ash about 2 per cent, acid-insoluble ash about 0.15 per cent. It is a hemostatic and blood coagulant.

VITACEÆ, OR VINE FAMILY

Shrubs, usually climbing by tendrils, with small, regular, greenish, usually polygamous flowers, the stamens as many as the valvate petals and opposite them; leaves alternate, palmate or compound; tendrils and flower clusters opposite the leaves. The most important genus is *Vitis* or Grape, species of which are widely cultivated throughout the temperate climate of the world.

Raisins (U. S. P. 1820 to 1882) are the dried mature fruit of *Vitis vinifera* Linné. The European Wine Grape, indigenous to western Asia, has been widely cultivated in Europe from a very early period, and in California since the Spaniards introduced it. As the grapes ripen, the stems are partially cut across and the fruit then partially dries as it ripens. After several weeks the bunches of fruit are cut off and fully dried in the sun; or the fully ripened fresh fruit is cut from the vine and dried on floors or platforms in the sun.

Spanish and Italian (Malaga) raisins usually are marketed in bunches, while California raisins are usually mechanically stripped from the bunches, de-seeded and tightly packed in cartons. Sultana raisins are smaller than Malaga raisins, light-colored and seedless. Corinthian raisins, improperly called currants, are much smaller, very dark in color.

Raisins contain grape sugar and potassium bitartrate. The seed yield about 10 per cent of a bland oil. Raisins are nutritive and demulcent and are used as a flavoring agent in starchy or mucilaginous infusions.

WHITE WINES—

Vinum or Wine, U. S. P. 1820 to 1851.
Vinum Album or White Wine, U. S. P. 1851 to 1863, 1882 to 1916.
Vinum Xericum or Sherry Wine, U. S. P. 1863 to 1882; N. F. 1916 to 1926, 1947 to date.

RED WINES—

Vinum Rubrum or Red Wine, U. S. P. 1851 to 1863, 1882 to 1916.
Vinum Portense or Port Wine, U. S. P. 1863 to 1882.

BRANDY—

Spiritus Vini Gallici or French Brandy, U. S. P. 1851 to 1916.

Spiritus Vini Vitis or Brandy, U. S. P. 1826 to 1947; N. F. 1947 to date.

Fresh ripe grapes separate under pressure into juice or "must" and husk-seeds or "marc." If the juice is fermented after filtration, a light-colored wine is produced; if it be fermented before filtration, a dark colored or red wine is formed.

The amount of sugar in grapes (dextrose) varies from 12 to 30 per cent, the larger quantity being produced in warmer climates. The alcohol formed by fermentation of the sugar may eventually stop the yeast activity; in grapes with but little sugar, it is all fermented and a **sour** or **dry** wine results; where there is an excess of sugar a **sweet** wine is formed. If wine is bottled before fermentation has ceased, carbonic acid is retained in the wine to form **sparkling** wine, as distinguished from **still** wine. As 10 to 12 per cent of alcohol stops fermentation, wine is usually **fortified** by adding grape brandy or alcohol. Finally wine is **clarified,** usually by precipitation methods using gypsum, gelatin, etc. It is especially desirable to remove all of the tannin. Pasteur introduced sterilization of certain wines as a preservative measure against acetic fermentation.

Wine is used medicinally as a mild stimulant and tonic.

Brandy is an alcoholic liquid obtained by the distillation of the fermented juice of sound ripe grapes and containing at 15.56° C. from 48 to 54 per cent, by volume, of C_2H_5OH. It must have been stored in wood containers for a period of not less than two years. Brandy meets the requirements of the tests of the National Formulary.

Brandy is used as a prompt stimulant in many forms of debility.

Argol or Crude Tartar is formed as a deposit in wine casks after the alcoholic fermentation of grape juice. It consists of potassium bitartrate with some calcium tartrate, coloring matter and extractive. Potassium bitartrate is soluble in 165 parts of cool water and is nearly insoluble in alcohol, hence its precipitation in the wine casks. Argol from red wines is quite highly colored. Argol is used almost exclusively for the preparation of **cream of tartar** and of **tartaric acid.**

MALVACEÆ, OR MALLOW FAMILY

This is a family of about 50 genera and 1000 species, widely distributed. The plants are mostly herbs, with simple leaves, regular flowers (having the stamens united into a column, which encloses the styles) and a capsular fruit. The mucilage secretory organs are characteristic: (A) epidermal cells in which the walls become metamorphosed to mucilage; (B) parenchyma cells in the axis and leaves in which the walls undergo a mucilaginous modification; (C) lysigenous mucilaginous cavities which are sometimes differentiated as canals and occur in the pith and the cortex. In the roots of *Althæa* the walls of the parenchyma cells of the vascular bundles are likewise modified to mucilage. Secretory cavities of schizogenous origin, and containing a yellow or yellowish brown amorphous substance, are found in *Gossypium* and some other genera. Non-glandular hairs, usually stellate, and glandular hairs of various forms in the different genera are frequently present.

ALTHEA

Althea or Marsh Mallow Root (U. S. P. 1831 to 1947; N. F. 1947 to date) is the dried root of *Althæa officinalis* Linné, derived of the brown corky layer and small roots. *Althæa* is from the Greek and means curing or cooling, in reference to the medicinal qualities. The plant is a perennial herb with erect woolly stems attaining the height of about one meter, indigenous to central Europe and has been naturalized in the United States, occurring in the marshes from Massachusetts to Pennsylvania.

The commercial supply is from Germany, France and Holland. The roots are collected in the autumn from plants of the second year's growth. Frequently the root is cut into small cubical pieces about 5 mm. in diameter, having a uniform grayish white color. Althea was described by Dioscorides. Charlemagne (742 to 814 A.D.) commanded that it be cultivated in his domain.

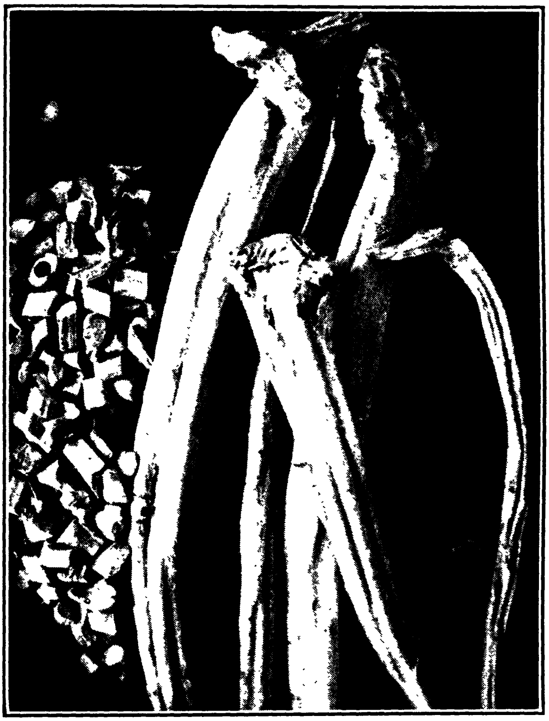


FIG. 226.—Commercial Althea Root. The whole peeled root and the cut root. (Photo by P. D. Carpenter.)

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 226, 227 and the National Formulary.

CONSTITUENTS.—Mucilage, 25 to 35 per cent; asparagin (amido-succinamide), 1 to 2 per cent; starch, about 35 per cent; pectin, about 10 per cent; sugar, about 10 per cent; ash, about 5 per cent.

Asparagin (β-asparagin, the monamide of aspartic acid) is an amido compound which is widely distributed throughout the vegetable kingdom. It is found in reserve organs, such as the tubers of potato and dahlia, the roots of althea, belladonna, etc., and the seeds of the chestnut tree, also in young shoots, such as those of asparagus, and in peas, beans, and other members of *Leguminosæ*. Asparagin has also been detected in some of the fungi, including the *Agaricineæ* and certain of the *Myxomycetes*. It is a plastic product playing a very important rôle in plant metabolism. It forms crystals up to 0.5 mm. long from the expressed uices or by mounting sections of them in glycerin. It has an acid reaction, is nsoluble in alcohol, but soluble in 47 parts of water at 17.5° C. and in 1.9 parts f distilled water at 98° C. It occurs in two forms, which are dextrorotatory nd levorotatory; the latter usually present in plants. Asparagin appears when roteins are being utilized by the plant, and also when they are being formed y the plant.

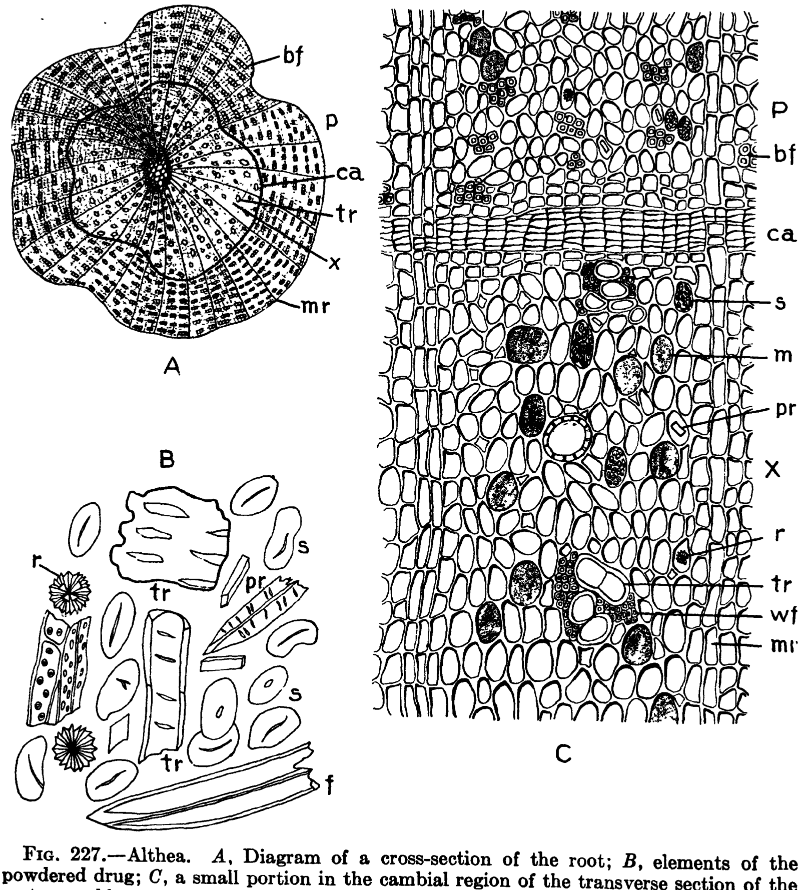


FIG. 227.—Althea. *A*, Diagram of a cross-section of the root; *B*, elements of the powdered drug; *C*, a small portion in the cambial region of the transverse section of the root: *p*, phloem area, containing numerous small bundles of bast fibers (*bf*) arranged in more or less concentric circles, numerous mucilage cells (*m*), and starch- or crystal-bearing parenchyma; *mr*, medullary rays, 1 or 2 cells wide, of starch-bearing parenchyma; *ca*, cambium, distinct in the smoothed transverse surface and in the section; x, xylem rays, composed mostly of thin-walled starch-bearing parenchyma and mucilage cells, but a few tracheæ (*tr*) with bordered pores, or scaariform markings are present; starch grains (*s*) numerous, ellipsoidal or irregular, up to 30 microns long and frequently with a long central cleft; bast fibers (*bf* and *f*) long, narrow, walls thickened, non-porous and more or less lignified; calcium oxalate crystals few, in prisms (*pr*) or rosettes (*r*) up to 35 microns in diameter. (Drawing by Edward Fried.)

STANDARDS AND TESTS.—Althea contains not more than 1 per cent of foreign organic matter. When 1 gm. of comminuted althea is macerated in 10 cc. of water for thirty minutes and then filtered through cotton, it yields a mucilage of pale yellow color which is neutral to litmus and which assumes a deep yellow color when treated with sodium hydroxide T.S. This latter mixture does not have a sour or an ammoniacal odor.

Uses and Dose.—Althea is a demulcent, administered *ad libitum;* it is used as an excipient in making pills, and for other pharmaceutical and food uses.

Marshmallow Leaves or Althæa Folia (U. S. P. 1831 to 1842; N. F. 1916 to 1936) consists of the dried leaves of *Althæa officinalis.* They are broadly ovate, petiolate, 3 to 10 cm. broad, with acute apex, cordate base, dentate, somewhat lobed margin, and surfaces velvety pubescent; inodorous and mucilaginous.

The powdered drug is grayish green, with numerous non-lignified stellate hairs, in clusters and up to 600 microns long; calcium oxalate rosettes up to 30 microns in diameter; epidermal fragments with stomata up to 37 microns long; a few spiny pollen grains; and numerous, large mucilage cells with highly refractile contents. The drug is used as a demulcent and emollient.

Marshmallow Flowers or Althæa Flores (U. S. P. 1851 to 1863) consists of the open flowers of *Althæa officinalis.* The flowers, like the leaves, are rich in mucilage, up to 16 per cent of the dry weight, and are used only for their demulcent and emollient properties.

Mallow Leaves or Malvæ Folia (N. F. 1916 to 1936) consists of the dried leaves of *Malva sylvestris* and *Malva rotundifolia.* The leaves are long petiolate, orbicular or reniform, slightly truncate or cordate at the base, 10 to 20 cm. in length, with 3 to 7 shallow, angular or rounded lobes, palmate venation, crenate-dentate margins, pubescent on both sides; inodorous; taste very mucilaginous.

In the powder non-glandular hairs up to 1 mm. in length, calcium oxalate rosettes, and large refractive mucilage cells are numerous. The dried drug contains up to 20 per cent of mucilage, 16 per cent of total ash, and about 0.3 per cent of acid insoluble ash. It is used as a demulcent and emollient.

The roots of a number of other genera of this family are used for similar purposes as althea; such as those of *Kosteletzyka pentacarpa* of southern Europe; *Hibiscus bancroftianus* of the West Indies; *Malvaviscus pentacarpus* of Mexico; *H. rosa-sinensis* of tropical Asia and cultivated; *Althæa rosea* of the Levant and cultivated, and *Sida ovalis* of Peru. Mucilage is also found in the flowers and leaves of one or more species of *Malva, Sida, Pavonia, Hibiscus, Pachira* and *Ceiba.*

COTTON

Purified Cotton or Absorbent Cotton (U. S. P. 1851 to date) is the hair of the seed of cultivated varieties of *Gossypium hirsutum* Linné or of other species of *Gossypium,* freed from adhering impurities, deprived of fatty matter, bleached and sterilized. *Gossypium,* the ancient name for the cotton plant, is from the Arabic *gos* meaning a soft silky substance; *hirsutum* is from the Latin meaning rough or hairy.

G. hirsutum, as cultivated in the southern United States, is an annual herb attaining a maximum height of about 4 feet, and yields most of the commercial cotton known as American Upland Cotton; *G. barbadense,* a somewhat larger plant, is cultivated in South Carolina and Georgia along the sea coast, and yields Sea Island Cotton.

The plants produce capsules (bolls) which open when ripe along longitudinal sutures, revealing a mass of white hairs attached to the brownish seed. The mass of hairs (cotton fibers) and seed is collected and "ginned," a machine process of removing the seed. To render cotton absorbent and suitable for surgical use, it is first carded (combed) to remove gross impurities and short hairs (linters), then washed with weak alkali solution to remove fatty materials, then bleached with chlorinated soda, washed with weak acid and then with water and finally dried and recarded into flat sheets. After the absorbent cotton is packaged, it is usually sterilized.

Cotton for textiles is spun into thread and then woven, or it may be treated with various chemicals, when it yields such fabrics as mercerized cotton, rayons and others. The United States produces about half the supply of cotton of the world. Cotton is also produced in Egypt and other tropical parts of Africa, India, the West and East Indies and South America.

Cotton has been known since remotest antiquity. It has been cultivated in India for more than 3000 years. Egypt had a well developed cotton industry 4000 years ago. It has been found in the mounds of the Aztecs in Mexico, which probably antedate the pyramids of Egypt.

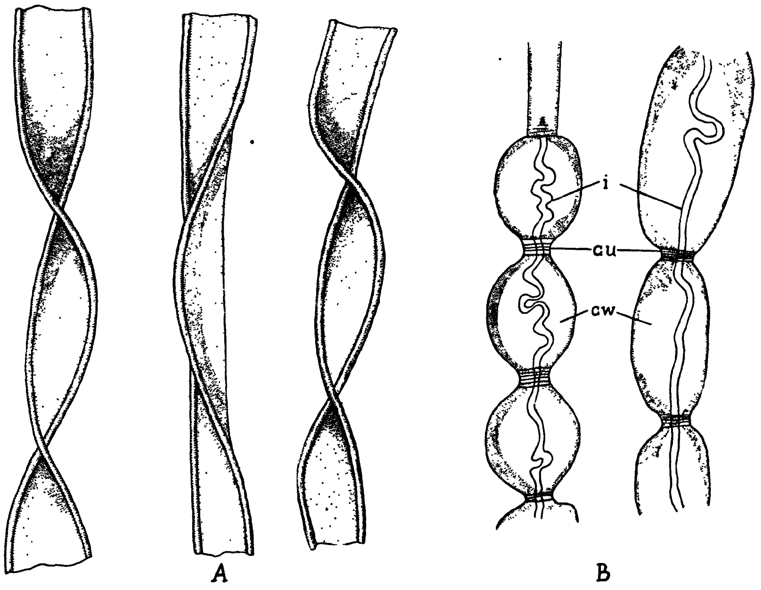


Fig. 228.—Cottonseed hairs: *A*, the normal flattened, twisted hairs; *B*, the hairs after treatment with cuprammonia showing cellulose cell wall swollen by the reagent (*cw*); encircling rings of the cuticle which is not swollen (*cu*); and inner membrane lining of the cavity (*i*). (Drawing by Edward Fried.)

Description.—A white, soft, tufted mass, consisting of somewhat flattened, twisted and spirally striate, 1-celled, non-glandular hairs, from 2.5 to 4.5 cm. in length and 25 to 35 microns in diameter; inodorous and tasteless.

Constituents.—Absorbent cotton, consisting almost exclusively of cellulose, is soluble in ammoniated cupric oxide T.S.

Standards and Tests.—Purified cotton yields not more than 0.2 per cent of ash and should be free from alkali, acid, fatty matter, dyes and water-soluble substances. Consult the U. S. Pharmacopœia for the methods of detecting these; also the tests for fiber length, sterility and absorbency.

Uses.—Absorbent cotton (sterilized) is employed as a surgical dressing where it serves for mechanical protection, to absorb blood, mucus or pus, and to keep bacteria from infecting the wounds. Commercially, cotton is employed for textiles and as a source of pure cellulose in the manufacture of explosives, celluloid, etc.

ADULTERANTS.—Various substances may be added to absorbent cotton to increase the rate of absorption of water, as chlorides of calcium, magnesium and zinc, glycerin and glucose; loading materials, as barium and calcium salts, and clay are added to inferior grades of the article.

The hairs from immature seeds are known as "dead cotton" and are distinguished by having very thin walls and a thin outer layer of cutin. They lack the essential properties for technical uses.

Absorbent Gauze, Gauze, Plain Gauze or Non-sterilized Absorbent Gauze (U. S. P. 1942 to date) consists of well-bleached cotton cloth of plain weave. It is white cotton cloth of various thread counts and weights. The ash does not exceed 0.15 per cent of the weight of the gauze. The Pharmacopœial tests prohibit or greatly limit the presence of dyes, fatty matter, dextrin or starch, acid, alkali and water extract in the gauze. Tests are provided for thread count, weight and absorbency of the gauze.

Sterile Absorbent Gauze, Gauze (U. S. P. 1942 to date) is absorbent gauze which has been rendered sterile and protected from contamination. The Pharmacopœia requires that each unit of sterile gauze be packed individually so that the sterility of the unit be maintained until the package is opened for use.

Adhesive Absorbent Gauze or Adhesive Gauze is an individual dressing prepared by affixing a plain absorbent compress to a strip of adhesive plaster. It must be sterile and each unit protected from contamination by suitable packaging.

Carbolized Gauze (N. F. 1888 to 1906) is prepared by immersing loosely-folded pieces of gauze muslin in an alcoholic solution of resin, castor oil and phenol, and pressing out the gauze until its weight is 170 parts for every 100 parts of dry gauze. Preserve in air-tight containers. It contains when dry about 2.5 per cent of phenol.

Iodoform Gauze (N. F. 1888 to 1906) is prepared by immersing a weighed quantity of gauze sufficient to absorb the following mixture: a solution of ten parts of iodoform in 40 parts of ether, alcohol 40 parts, glycerin 5 parts and tincture of benzoin 5 parts. The gauze is dried and preserved in tight receptacles

Gauze Bandage or Roller Gauze Bandage (U. S. P. 1942 to date) is prepared from Type I Absorbent Gauze in various widths and lengths. Each bandage is in one continuous piece, tightly rolled and substantially free from loose threads and ravelings. Gauze bandage must be sterile and protected from contamination.

Cottonseed Oil (U. S. P. 1882 to date) is the refined fixed oil obtained from the seed of cultivated plants of various varieties of *Gossypium hirsutum* Linné or of other species of *Gossypium*. The cotton seed, after ginning off the fibers, is decorticated, cleaned of hulls, the kernels steamed and pressed at about 1500 pounds pressure to yield about 30 per cent of oil. The oil thus obtained is turbid and reddish in color; it is refined by filtering, decolorizing and "winter chilling" which removes the stearin.

DESCRIPTION.—Cottonseed oil is a pale yellow, oily liquid. It is odorless and has a bland taste. Consult the U. S. Pharmacopœia for characteristics and tests.

CONSTITUENTS.—Cottonseed oil consists largely of olein with small quantities of palmitin and stearin or the corresponding fatty acids, which, however, are largely removed in well-purified oil.

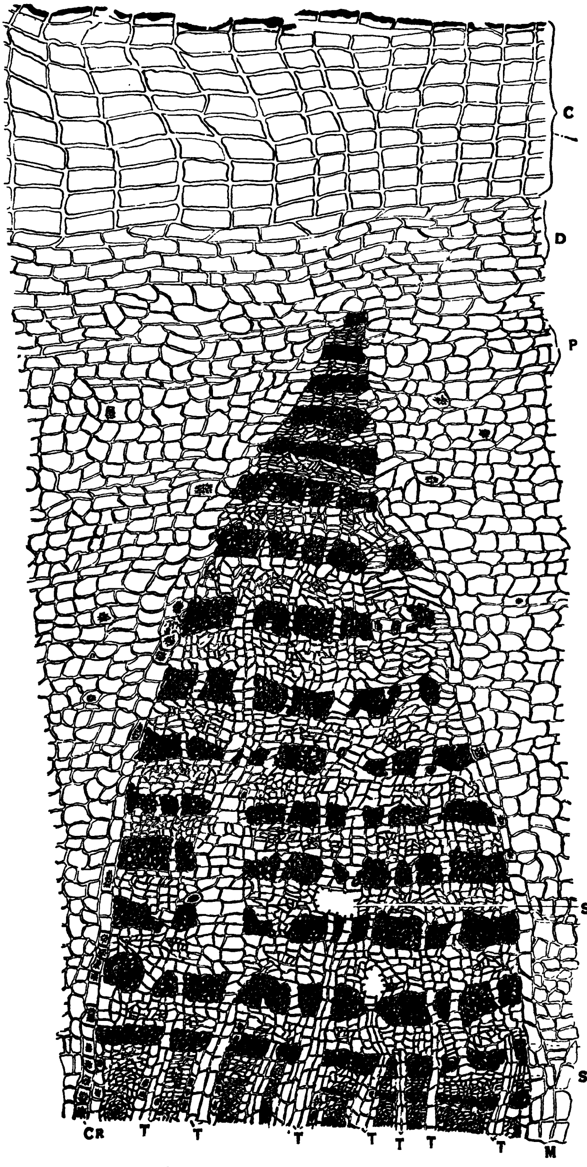


FIG. 229.—Transverse section of cotton root bark showing the characteristic cone-shaped strands of phloem: *C*, layers of cork, consisting of rectangular tabular cells with thin yellowish brown walls; *D*, tannin-bearing cells of cortex; *P*, parenchyma of primary medullary ray (*M*) with occasional calcium oxalate rosettes (*Cr*); *B*, bast; *Sc*, secretory cavities; *T*, secondary medullary rays; *S*, sieve. (After Morgan.)

Uses and Dose.—Cottonseed oil is a bland, nutritious oil and is used in liniments on account of its emollient properties. The oil is employed in place of olive oil as a cooking and salad oil. A considerable quantity is hydrogenated and used in making substitutes for lard. A large amount is also used in the manufacture of soap. About 200,000,000 gallons of cottonseed oil are produced in the United States annually.

Cottonseed Cake contains about 0.6 per cent of a toxic principle, gossypiol, which occurs in secretory cavities in all parts of the plant. It is present in cold pressed oil from which it may be removed by treatment with alkalis.

Cotton Root Bark (U. S. P. 1863 to 1916; N. F. 1916 to date) is the recently gathered, air-dried bark of the root of one or more of the cultivated varieties of *Gossypium hirsutum* Linné, or of other species of *Gossypium*. Most of the commercial supplies come from Virginia, the Carolinas and other cotton growing states.

Description.—In flexible bands or in transversely curved or slightly quilled pieces, the bark 0.5 to 1 mm. in thickness; outer surface light brown, longitudinally wrinkled, with small lenticels, periderm frequently exfoliated; inner surface light brown, longitudinally striate; fracture tough, fibrous; readily separable into fibrous layers.

Powder.—Light brown; odor faint; taste slightly acrid; bast fibers up to 1 mm. in length, about 15 microns in width, the walls strongly lignified and with very few pores, the ends being acute or markedly attenuate; starch grains somewhat spheroidal, from 3 to 20 microns in diameter, single or compound; parenchymatous cells with irregular yellowish and reddish tannin masses or filled with starch; calcium oxalate crystals in rosettes from 10 to 25 microns in diameter.

Constituents.—About 8 per cent of a peculiar, colorless acid resin, which is soluble in water and becomes reddish and insoluble on exposure to the air; hence, the drug, promptly after drying, should be prepared into fluidextract to preserve its activity. It also contains fixed oil; tannin; starch and calcium oxalate. Total ash, about 4.8 per cent.

Uses and Dose.—The drug is an emmenagogue and an oxytocic. Average dose, 2 gm.

The **flowers** of the cotton plant contain an interesting glucoside, gossypetin, which becomes green on oxidation and is colored orange red with solutions of alkalis. It somewhat resembles a similar principle found in arbor vitæ (*Thuja occidentalis*).

STERCULIACEÆ, OR COLA FAMILY

This is a family of about 58 genera and 660 species of tropical and subtropical plants. They comprise a great many forms, some being lianes. They resemble the *Malvaceæ* very closely and are distinguished by their 2-locular anthers. The mucilage secretory organs occur as mucilaginous membranes, as lysigenous mucilaginous cavities and as schizogenous or lysigenous canals. In addition, tannin-secretion cells are usually present. Non-glandular hairs, although usually stellate, peltate or tufted, may occur in other specific forms. The glandular hairs are either unicellular or made up of a few cells, and somewhat resemble those of the *Malvaceæ*.

THEOBROMA

Cacao Seeds or Cacao Beans are the roasted seed of *Theobroma Cacao* Linné. *Theobroma* from the Greek means "food of the gods;" *cacao* is from the Aztec name of the tree; "chocolate" is from the Mexican, and it has long been highly esteemed by the Aztecs and the Mexicans, and later by the Europeans who learned of it from them.

The plant is a tree attaining the height of about 12 meters and is indigenous to Mexico but widely cultivated in tropical countries. The flowers arise from the older branches or trunk, developing into a large, ovoid, fleshy fruit which is 10-furrowed longitudinally, yellow or reddish, and contains five rows of seeds, 10 or 12 in each row (Fig. 230). Cacao was known to Columbus and Cortez. Most of the cacao seed of the market is obtained from Ecuador (the Guayaquil variety being especially valuable), Curaçao, Mexico, Trinidad, Central America, Brazil, West Africa (Nigeria and the Gold Coast), Ceylon, Java and the Philippine Islands.

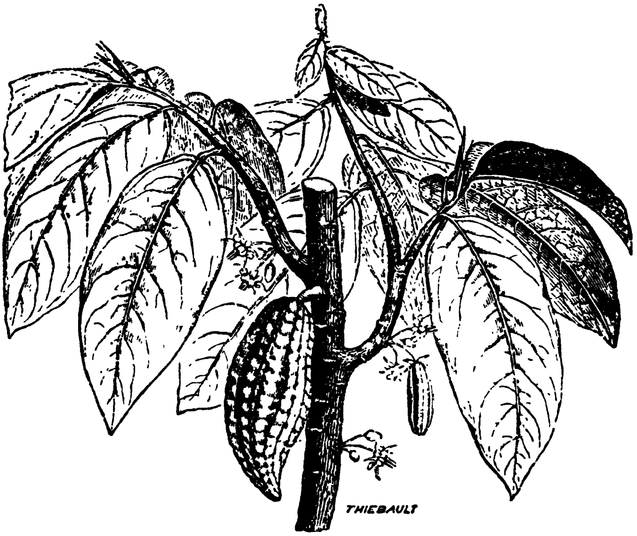


FIG. 230.—Cacao tree (*Theobroma cacao*) showing the peculiar habit of the fruits in developing on the main axis as well as on the branches. (After Baillon.)

The seeds are separated from the pod and allowed to ferment, changing during the process from white to dark reddish brown. They are then roasted (not above 140° C.) losing water and developing their characteristic odor and taste. The roasted seed are passed through a "nibbling" machine to crack the seed coats (**Cacao Shells**) which are separated from the kernels by winnowing. The broken kernels are called "nibs," and when ground between hot rollers they yield a paste containing up to 50 per cent of fat, **Cacao Butter.** The paste congeals at room temperature to form **Bitter Chocolate. Sweet Chocolate** is bitter chocolate to which sugar and vanilla or other flavoring substances have been added. After expressing cacao butter, the marc, retaining some oil, is powdered and known as **Prepared Cacao,** or **Breakfast Cocoa.** Some brands of cocoa contain alkali to render it "soluble;" it is, of course, not soluble, but the alkali partially saponifies the fat at the surface of each minute particle, resulting in a smoother and more complete suspension of the cocoa in the water or milk of the drink.

Cacao Seeds or Cacao Beans are often found on the market as such. The seed is irregularly ellipsoidal or ovoid, somewhat flattened, from 15 to 30 mm. in length; externally reddish brown to dark brown; seed coat thin and shell-like, readily separable from the cotyledons; the latter are very fleshy, much folded and connected with a stout radicle, situated at the hilum portion of the seed; odor chocolate-like, and taste slightly bitter.

The seeds contain 35 to 50 per cent of a fixed oil; about 15 per cent of starch; 15 per cent of proteins; 1 to 4 per cent of theobromine; 0.07 to 0.36 per cent of caffeine; about 0.5 per cent of sugar; and a small amount of tannin. The red color of the seed is due to a principle known as cacao-red, which is formed by the action of a ferment on a glucoside. When the seeds are roasted the theobromine present in the kernel passes into the shell, the latter being the commercial source of the alkaloid.

Theobromine is an alkaloid, 3, 7-dimethylxanthine ($C_7H_8O_2N_4$) obtained from cacao seed, or rather cacao shells after the roasting of the seeds. It is also present in Kola nut.

The alkaloid is slightly soluble in cold water, 1 to 2000, or in alcohol 1 to 2200, but becomes readily soluble in water when combined with bases. Dose, 0.3 to 0.5 gm.

Theobromine and Sodium Salicylate (U. S. P. 1916 to 1942; N. F. 1942 to date) is a hydrated mixture of theobromine sodium and sodium salicylate in approximately molecular proportions. When dried at 110° C., it yields not less than 46.5 per cent of anhydrous theobromine and not less than 35 per cent salicylic acid. It is a white, odorless powder having a sweetish, saline and somewhat alkaline taste. It is soluble in one part of water; if the mixture absorbs carbon dioxide with the liberation of theobromine, it becomes incompletely soluble in water. Average dose, 1 gm.

Theobromine and Sodium Acetate (U. S. P. 1942 to date) is a hydrated mixture of theobromine sodium and sodium acetate in approximately molecular proportions. It contains not less than 55 per cent and not more than 65 per cent of anhydrous theobromine. It is a white, crystalline powder, practically odorless, and of a bitter taste. It is soluble in 1.5 parts of water and is alkaline in reaction. Average dose, 0.5 gm.

Theobromine is a diuretic and myocardial stimulant; it has but little stimulant action on the central nervous system, hence is preferred over caffeine in cardiac edemas and to relieve the pain of angina pectoris.

Cacao Butter (U. S. P.1863 to date) is a yellowish white solid, having a faint, agreeable odor and a bland chocolate-like taste, melting between 30° and 35° C. It consists of the glycerides of stearic, palmitic, arachic, oleic, and other acids, usually in mixed glyceride formation. Specific gravity, 0.858 to 0.864 at 100°/25° C.; refractive index, 1.4537 to 1.4578 at 40° C.; saponification value not less than 188° and not more than 195°; iodine value not less than 35 and not more than 40; the fatty acids solidify between 45° and 50° C. Cacao butter must be free from wax, stearin or tallow.

Cacao butter is used pharmaceutically almost entirely for making suppositories.

Cacao, Powdered Cocoa (N. F. 1916 to date) is a powder prepared from the roasted, cured kernels of the ripe seed of *Theobroma Cacao* Linné.

DESCRIPTION.—**Cacao** is reddish brown, and consists chiefly of protein grains, oil and starch grains (Fig. 231), the latter up to 15 microns in diameter; fragments with brownish or purplish brown contents (cacao-red); and crystals of cacao butter in small prisms or needles. A few fragments of seed coat consisting of hexagonal epidermal cells and a peculiar mucilage layer of small tubular cells and a layer of nearly isodiametric stone cells about 10 microns in diameter may be present.

Standards and Tests.—Cacao yields not more than 22 per cent of non-volatile, ether-soluble extractive, which does not have a spicy odor or taste The ether-insoluble residue, dried to constant weight, yields not more than 7 per cent of crude fiber, not more than 8 per cent of total ash, and not more than 0.4 per cent of acid-insoluble ash. It shows, microscopically, not more than 3 per cent of cacao shells and not more than 15 per cent of starch.

Uses.—Cacao is a nervine and a stimulant; it is used chiefly in the form of a beverage and as a flavoring agent.

Cacao Shells are used as such, or admixed with cocoa, to form a cheap grade of cocoa. These may be detected when as low as 1 per cent are present by a fluorescence shown under the microfluoroscope. Cereal starches or starchy products have been used as an adulterant for cocoa, but rarely so now.

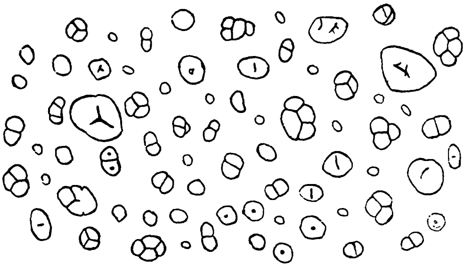


Fig. 231.—Cacoa starch: starch grains of commercial cacao powder, or chocolate, after removal of the oil by means of ether.

KOLA

Kola, Cola or Kolanuts (N. F. 1916 to date) is the dried cotyledon of *Cola nitida* (Ventenat) Schott and Endlicher, or of other species of *Cola*. It yields not less than 1 per cent of anhydrous caffeine. The African name of the drug is Cola. The plant is a large tree indigenous to West Africa between Sierra Leone and the Congo. It is now cultivated in East Africa, Ceylon, Java, Brazil and the West Indies. The fruit is a pod 5 or 6 inches long, which slowly dehisces, when the seeds are carefully collected, dried and packed. The commercial supplies come principally from western Africa and the West Indies, the latter being known commercially as **Bichy** or **Bissy-bissy Nut.**

Description.—Cotyledons, irregularly plano-convex or polygonal, 2 to 5 cm. in length, brown, nearly smooth, heavy, hard and tough, the edges slightly recurved and sharp.

Powder.—Light brown to moderate yellowish brown; odor characteristic; taste astringent, somewhat sweet; starch grains numerous, up to 45 microns in diameter, spheroidal, ellipsoidal or shell-shaped, some with a central hilum or cleft and a distinct cross under the micropolariscope; parenchyma cells mostly with reddish brown walls.

Constituents.—Caffeine, up to 3.5 per cent; theobromine, less than 1 per cent; starch abundant; a lipase and a small amount of tannin; total ash, about 3 per cent. In the fresh nuts the caffeine is combined with a tannin-like substance which neutralizes its activity; when the nuts are dried the caffeine assumes its activity.

Caffeine may readily be isolated from kola by microsublimation (see Fig. 232). This may then be further identified by the gold chloride reaction (see Fig. 233). If sections of kola are mounted in hydrochloric acid and a drop of 5 per cent gold-chloride solution added to the mount, crystals of the caffeine-gold-chloride combination will be formed.

USES AND DOSE.—Kola has the action of caffeine; it is a nervine, a stimulant, also a tonic and an astringent. Average dose, 4 gm.

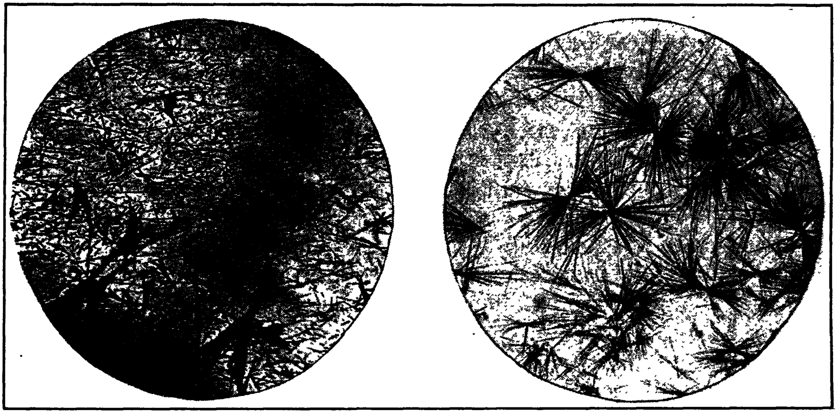


FIG. 232 FIG. 233

FIG. 232.—The sublimate of caffeine from powdered kola.

FIG. 233.—Crystals of caffeine-gold-chloride obtained by treating the sublimate with 5 per cent gold chloride solution. (Photomicrographs by Adamson.)

ALLIED PRODUCTS.—The seeds of a number of other plants are said to be sometimes admixed with kola and of these the following may be mentioned: *Cola ballayi*, a plant growing in the Gaboon, the seeds of which contain 6 cotyledons and are deficient in alkaloids. The seeds of *Garcinia cola* (Fam. *Guttiferæ*) have been substituted for kola under the name of "Staminate Cola." These seeds do not contain caffeine, but contain two resins which seem to have a physiological effect similar to that of cola. The seeds of *Pentadesma butyraceum*, of Sierra Leone, have also been used as a substitute for kola; they contain a fat, having a turpentine-like odor, which is used by the natives in place of butter, and hence the tree is known as the "Butter" or "Tallow" tree.

CAFFEINE

Caffeine (U. S. P. 1882 to date), 1, 3, 7-trimethylxanthine, $C_8H_{10}O_2N_4.H_2O$ occurs in coffee, tea, cacao, guarana and maté as well as in kola. While caffeine can be produced synthetically, it is usually prepared from tea, tea dust or tea sweepings, or recovered from coffee roasters. Caffeine is anhydrous, or contains not more than 8 per cent of water of hydration.

DESCRIPTION.—Caffeine occurs in white, flexible, silky, acicular crystals, usually matted together in fleecy masses and having a bitter taste. Caffeine may be sublimed without decomposition on heating. On treating a small quantity of caffeine with a few drops of nitric acid or chlorine water and evaporating the solution to dryness on a water-bath, the reddish yellow residue is colored purplish by ammonia. A similar reaction is also obtained by treating the alkaloid with hydrochloric acid and a crystal of potassium chlorate, evaporating the solution and adding a drop of ammonia water to the residue; or exposing to ammonia vapors; this is known as the **murexide reaction.** Caffeine may be identified microchemically by adding a drop of hydrochloric acid and a drop of 5 per cent solution of gold chloride. The resulting crystals are needles which occur in spheroidal aggregates or in fan-shaped branching groups (see Fig. 233). Caffeine should be free from carbonizable substances and from other alkaloids. Consult the U. S. Pharmacopœia for solubilities, etc.

USES AND DOSE.—Caffeine is a nervine and stimulant. Average dose, 0.2 gm.

Citrated Caffeine (U. S. P. 1894 to date) is a mixture in about equal proportions of caffeine with citric acid. Average dose, 0.3 gm.

Caffeine and Sodium Benzoate or Caffeine Sodio-benzoate (N. F. 1888 to 1916; U. S. P. 1916 to date) is a mixture of caffeine and sodium benzoate, which contains, when dried at 80° C. to constant weight, not less than 47 per cent and not more than 50 per cent of anhydrous caffeine, and not less than 50 per cent and not more than 53 per cent of sodium benzoate. The sum of the percentages is not less than 98 per cent and not more than 102 per cent. Average dose, 0.5 gm.

Caffeine and Sodium Salicylate or Caffeine Sodio-salicylate (N. F. 1888 to date) is a mixture of caffeine and sodium salicylate. When dried to constant weight at 80° C., it contains, in each 100 gm., not less than 48 gm. and not more than 52 gm. of caffeine, or of sodium salicylate. Average dose, 0.2 gm.

The solubility in water of caffeine is markedly increased by the presence of citric acid, benzoates, salicylates and bromides; caffeine and sodium benzoate is most suitable for hypodermic or intramuscular injection.

STERCULIA GUM

Sterculia Gum or Gum Karaya (N. F. 1947 to date) is the dried gummy exudation from *Sterculia urens* Roxburgh, *Sterculia villosa* Roxburgh, *Sterculia tragacantha* Lindley or other species of *Sterculia,* or from *Cochlospermum gossypium* DeCandolle or other species of *Cochlospermum* (Fam. *Bixaceæ*). These trees are native to India and are widely scattered in the Indian forests. They may attain a height of 10 meters, but the trunks are very large, soft and corky. Sterculia is from the Latin *Sterculius,* the deity that presided over manuring in reference to the fetid odor of the trees.

The gum exudes naturally or from incisions made to the heartwood, and is collected throughout the year, except in the rainy season, but mostly from March to June. The incisions produce knob-like masses of gum, which should be frequently collected for nine months, then the tree should rest for two or three years. Grading and shipping is done in Bombay.

DESCRIPTION.—Sterculia gum occurs in tears or irregular fragments with a crystalline appearance; it is pale yellow to pinkish brown, translucent and horny with a slight acetous odor. It swells in water and is insoluble in alcohol. Pieces of bark and very dark pieces of gum should be few. For constants and tests of identity and purity see the National Formulary.

STANDARDS.—Two gm. of the gum absorbs not less than 50 cc. of water; the moisture content does not exceed 20 per cent; no blue color is produced with iodine solution; foreign matter and bark does not exceed 3 per cent; the mucilage is more viscid but less adhesive than a corresponding mucilage of tragacanth.

USES.—Sterculia gum is a mechanical laxative and is used for emulsions and suspensions; it has a large use in finger-wave sets and in skin lotions; also in the textile and printing industries; in the preparation of food products; in the preparation of composite building materials, etc.

THEACEÆ, OR TEA FAMILY

The plants of this family numbering about 16 genera and 175 species are shrubs or trees with alternate, evergreen leaves and perfect regular flowers with numerous stamens, occurring one or more in the axils of the leaves. The fruit is a 3- to 5-locular dehiscent capsule. The most important member of the family is *Thea sinensis*, the two varieties *viridis* and *bohea* furnishing the leaves known as tea.

Thea or Tea consists of the prepared leaves and leaf-buds of *Thea sinensis*, a shrub or tree with alternate, evergreen leaves. The tea tree is indigneous to eastern Asia, and is now extensively cultivated in China, Japan, India and Java. The generic name is from the Greek meaning *goddess; sinensis* refers to its Chinese origin.

Green Tea is prepared in China and Japan by rapidly drying the freshly picked leaves in copper pans over a mild artificial heat. Often the leaves are rolled by the palm of the hand as they dry.

Black Tea is prepared in Ceylon and elsewhere by heaping the fresh leaves until fermentation has begun, then rapidly drying with artificial heat and mechanical means.

Tea occurs in more or less crumpled masses; bright green or blackish green; odor agreeable, aromatic; taste pleasantly astringent and bitter.

Tea leaves are distinguished from most other leaves by their large colorless stone cells or idioblasts, which frequently extend from the upper to the lower surfaces of the leaf. For the structure and powder, see Figure 234. Adulterants are chiefly distinguished by possessing other forms of calcium oxalate crystals and hairs.

Tea contains two alkaloids, caffeine (theine) 1 to 4 per cent, and theophylline in very small percentage; about 15 per cent of gallotannic acid; and about 0.75 per cent of a yellow volatile oil, solid at ordinary temperatures and having a strongly aromatic odor and taste. Total ash about 2.5 per cent.

Tea is an astringent; it is also a nervine and a stimulant. It is used mainly in infusion as a beverage.

Theophylline, Theocin or 1, 3-dimethylxanthine (U. S. P. 1916 to date) is isomeric with theobromine, and was first isolated from tea in 1885. It is prepared synthetically from caffeine or by other means. It occurs as a white, odorless, bitter crystalline powder and is soluble in about 120 parts of water.

Theophylline Ethylenediamine or Aminophylline (U. S. P. 1936 to date) is a compound containing approximately 79 per cent of anhydrous theophylline and 13 per cent of ethylenediamine. It occurs as white or slightly yellowish granules or powder, with a slight ammoniacal odor and a bitter taste. It is soluble in about 5 parts of water, the solution being alkaline to litmus paper.

Theophylline and Sodium Acetate (U. S. P. 1936 to date) is a hydrated mixture of theophylline sodium and sodium acetate in approximately molecular proportions. It yields not less than 55 per cent and not more than 65 per cent of anhydrous theophylline. It is soluble in about 25 parts of water, the solution being alkaline to phenolphthalein T. S.

The three items above may be used as stimulants like caffeine, but are used principally as diuretics. The mixtures of theophylline with alkaline materials render the alkaloid much more soluble in water, hence more suitable for hypodermic use. Average dose of each is 0.2 gm.

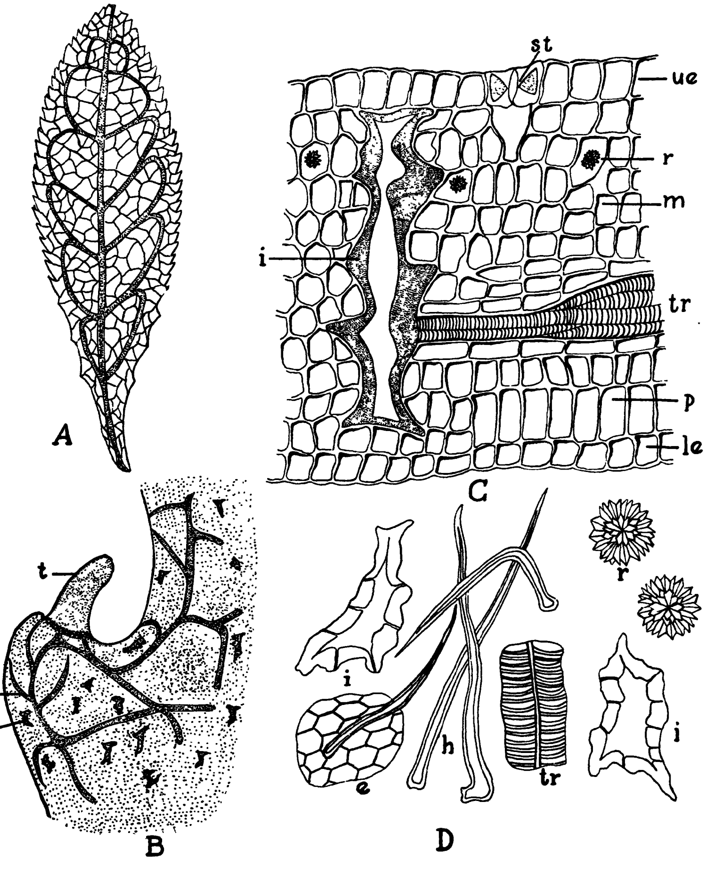


FIG. 234.—Tea Leaves: *A*, entire leaf showing venation and margin; *B*, a portion of the leaf cleared in chloral T.S. showing marginal tooth (*t*), veins (*v*) and idioblasts (*i*); *C*, transverse section through the blade of the leaf showing upper epidermis (*ue*) with stoma (*st*), mesophyll (*m*) containing rosettes of calcium oxalate (*r*), an occasional large elongated, irregular, somewhat branched, colorless stone cell or idioblast (*i*), and palisade (*p*); portion of a vein showing spiral tracheæ (*tr*); *le*, lower epidermis; *D*, elements from powdered tea including long non-glandular hairs (*h*) up to 10 microns in width, idioblasts (*i*), rosettes of calcium oxalate (*r*) about 10 microns in diameter, spiral tracheæ (*tr*), and a fragment of the epidermis showing a hair (*e*). (Drawing by Edward Fried.)

Maté or Paraguay Tea consists of the leaves of *Ilex paraguariensis* (Fam. *Aquifoliaceæ*), is distinguished by the stomata, which are much larger than the epidermal cells of the lower surface; the epidermal cells occurring near the veins are in nearly parallel rows and have a striated cuticle; sclerenchymatous fibers are associated with the tracheæ and calcium oxalate occurs in rosettes. Maté contains caffeine up to 2 per cent, volatile oil, tannin and matéviridic acid. It is laxative or purgative in large doses, stimulant, diaphoretic and diuretic. It is employed in South America in an infusion similar to tea, and is used to a considerable extent in a similar manner in the United States.

GUTTIFERÆ, OR GAMBOGE FAMILY

This is a family of about 45 genera and 900 species of tropical trees and shrubs. They all possess schizogenous resin canals in both the pith and the cortex. Resin cavities are also found in the leaves of certain genera. Lysigenous mucilage receptacles are present in *Quinia*. The tracheæ are marked by simple pores; the wood fibers may possess either simple or bordered pores; and wood parenchyma occurs in rather broad strands in the xylem. Calcium oxalate is usually secreted in the form of solitary crystals or rosettes; occasionally it occurs in small prismatic crystals, as in *Garcinia*. The stomata are especially characterized by having the neighboring cells parallel to the pore. Non-glandular hairs are either unicellular or uniseriate. Glandular hairs are wanting.

GAMBOGE

Gamboge (U. S. P. 1820 to 1936; N. F. 1936 to date) is the gum resin obtained from *Garcinia Hanburyi* Hooker filius. *Garcinia* is in honor of Laurent Garcin, a French botanist, and *Hanburyi* in honor of the English botanist, Hanbury. The tree attains a height of 15 meters in Cambodia, Siam and Cochin China, its habitat. Spiral incisions through the bark from the ground upward permit the resinous emulsion in the cortex and phlœm to exude. It is collected in bamboo nodes, and when solidified these are cracked open and the gamboge thus obtained is called Pipe Gamboge, the best commercial variety. That which hardens on the ground or is collected in leaves, known as Cake Gamboge, is more contaminated with dirt. The early Chinese regarded the drug as a poison and it was employed by them chiefly as a pigment. Its use as a purgative dates back to about 1600 A.D.

DESCRIPTION.—In cylindrical pieces, frequently hollow in the center, of variable length, 2 to 5 cm. in diameter; externally grayish orange brown, longitudinally striate; hard and brittle, the fractured surface somewhat conchoidal, orange red, waxy and somewhat porous.

POWDER.—Bright yellow; inodorous and sternutatory; taste very acrid; when mounted in chloral T.S., nearly all the particles slowly dissolve, leaving but a few fragments of vegetable tissue and very few or no starch grains; soluble in solutions of the alkalis with the production of an orange red color, and partially soluble in alcohol.

CONSTITUENTS.—Gum, allied to arabin, 15 to 20 per cent; a resin containing α-, β- and γ-garcinolic acids, known as cambogic acid, from 65 to 75 per cent; a volatile oil. Ash, 1 to 3 per cent with about 0.25 per cent acid-insoluble ash.

STANDARDS AND TESTS.—Gamboge contains not more than 1 per cent of foreign organic matter and yields not more than 1 per cent of acid-insoluble ash and not less than 65 per cent of alcohol-soluble extractive. When rubbed with water, gamboge yields a yellow emulsion which becomes darker and almost transparent upon the addition of ammonia water. The emulsion does not turn green upon the addition of iodine test solution.

Uses and Dose.—Gamboge is a drastic purgative or hydrogogue cathartic. Average dose, 0.125 gm. (cattle, 15 gm.).

Adulterants.—Gamboge is sometimes adulterated with vegetable fragments, inorganic substances (sand), and wheat or rice flour, which the powdered drug may contain to the extent of nearly 50 per cent.

Allied Products.—A drastic gum-resin is also obtained from *Garcinia morella* and other members of the *Guttiferæ* of India and Malaya, as *G. collina*, of New Caledonia; *Vismia laccifera*, of Brazil; *Clusia rosea*, of the West Indies and South America, and *Clusia macrocarpa*, of Guiana. Gamboge of a poor quality is obtained from *Arasina gurgi*, of India.

CISTACEÆ, OR ROCKROSE FAMILY

This is a family of low shrubs and herbs of which there are about 150 species. They are found chiefly in the northern countries of both hemispheres. They possess simple leaves, regular and perfect flowers and capsular fruits, and are especially characterized by their thick-walled unicellular hairs, which are frequently united, forming stellate groups. The glandular hairs are always uniseriate. The pericycle is a continuous ring including both stone cells and bast fibers. Calcium oxalate is secreted in the form of rosettes.

Helianthemum, Frostweed or Frost-wort (U. S. P. 1851 to 1882; N. F. 1916 to 1926) is the overground plant of *Helianthemum canadense*, a low shrub growing in dry, sandy soil from Massachusetts to North Carolina.

Frostweed contains a small quantity of volatile oil; 10 per cent of tannic acid; a bitter principle which forms white crystals; and probably also a glucoside. The presence of small crystals of ice at the base of the stem in autumn is due to the freezing of globules of water which have been deposited on the stellate hairs, hence the popular name "frostweed" is given to the plant. Helianthemum is used as a tonic, an astringent and an alterative.

BIXACEÆ, OR ANNATTO FAMILY

These are shrubs or trees found in the tropics and are of interest chiefly on account of the seeds of *Bixa orellana*, which furnish the coloring matter known as **Annatto (Orlean, Arnotta)**. The plant is found in tropical America and also in Polynesia and Madagascar. The seeds are covered with a fleshy arillus from which the coloring matter is prepared by means of water. The insoluble matter is collected, made into cakes and chiefly used for dyeing and coloring. Annatto contains a red crystalline principle, bixin, a yellow coloring principle, orellin and an ethereal oil. The root of this plant also contains some coloring matter.

FLACOURTIACEÆ

These are shrubs or small trees of tropical Africa and Asia, closely related to the Annatto family. There are about 70 genera and 500 species. Leaves simple, alternate, toothed or crenate; flowers in small racemes or panicles, diœcious, rarely showy; fruit a several-seeded berry, often edible.

CHAULMOOGRA

Chaulmoogra Seed is the ripe seed of *Taraktogenos Kurzii* King, *Hydnocarpus Wightiana* Blume, or *Hydnocarpus anthelmintica* Pierre. Chaulmoogra is the native Burmese name of the tree; *Taraktogenos* is Greek, meaning confused, as this genus was earlier confused with the genus *Hydnocarpus; Kurzii* is in honor of the botanist Sulpiz Kurz; and *Wightiana* is in honor of Wight. The plants are tall trees native to Burma, Siam and eastern India. The oil is "cold-pressed" from the kernels of the seed in Calcutta, which is the principal city of export.

Chaulmoogra Oil (U. S. P. 1826 to 1947; N. F. 1947 to date) is the fixed oil expressed from chaulmoogra seed. The fixed oil expressed from other species of *Hydnocarpus* when designated as such, and when conforming with the description, physical properties and tests for identity and purity prescribed by the National Formulary may be used.

Taraktogenos seed are irregularly ovoid, up to 2.5 cm. long, about one-half as thick; with a rather thin gray-brown testa, easily broken in commercial handling. The kernels yield up to 30 per cent of a fixed oil by expression. Hydnocarpus seed are about one-half as long and bear slight ridges radiating from the base. Their testa is thicker and not easily broken in commerce, hence the kernels are not so liable to deterioration. Hydnocarpus seed have been used medicinally in China and southeastern Asia for centuries.

The oil is a yellow or brownish yellow liquid, or at lower temperatures a soft, whitish mass, with a characteristic odor and somewhat acrid taste; it is sparingly soluble in alcohol but soluble in other fat solvents. Consult the National Formulary for its properties and constants.

CONSTITUENTS.—Mostly the glyceryl esters of highly unsaturated, optically active acids, principally chaulmoogric acid and hydnocarpic acid; these acids contain a closed 5-carbon ring, not found in other oils.

USES AND DOSE.—These fatty acids possess a specific toxicity for *Bacillus Lepræ* and *Bacillus Tuberculosis in vitro*, ten times as powerful as that of phenol. However, in the treatment of clinical leprosy and of clinical tuberculosis with the oil, sodium chaulmoograte, or ethyl chaulmoograte, the results have not been a marked success with either disease. Recent infections and cases of less than five years' standing are more amenable to improvement. Possibly the acids do not reach the bacteria imbedded in the tubercles or indurated tissues. The oil by mouth tends to cause nausea and intestinal irritation; by subcutaneous or intramuscular injection it tends to cause necrosis of the adjacent tissue. The salt and the ester are less irritant. Average dose, 1 cc.

Ethyl Chaulmoograte (U. S. P. 1926 to 1947; N. F. 1947 to date) consists of the ethyl esters of the mixed acids of chaulmoogra oil. It has the advantage over the oil of being less objectionable to the taste when taken orally, and less irritating locally when injected. Average dose, 1 cc.

CANELLACEÆ, OR CANELLA FAMILY

This is a small family of 4 genera, comprising in all about 8 species. They are mostly tropical or subtropical trees, having alternate evergreen leaves, golden yellow flowers and fleshy, berry-like fruits. The phelloderm is characteristic in that the inner walls of the cells are strongly lignified. The pericycle does not contain any sclerenchymatous tissue. Secretory cells, distributed throughout the parenchyma of stems, roots and leaves are spheroidal or ellipsoidal, possess suberized walls and contain a yellowish oily content. Both glandular and non-glandular hairs apparently are wanting.

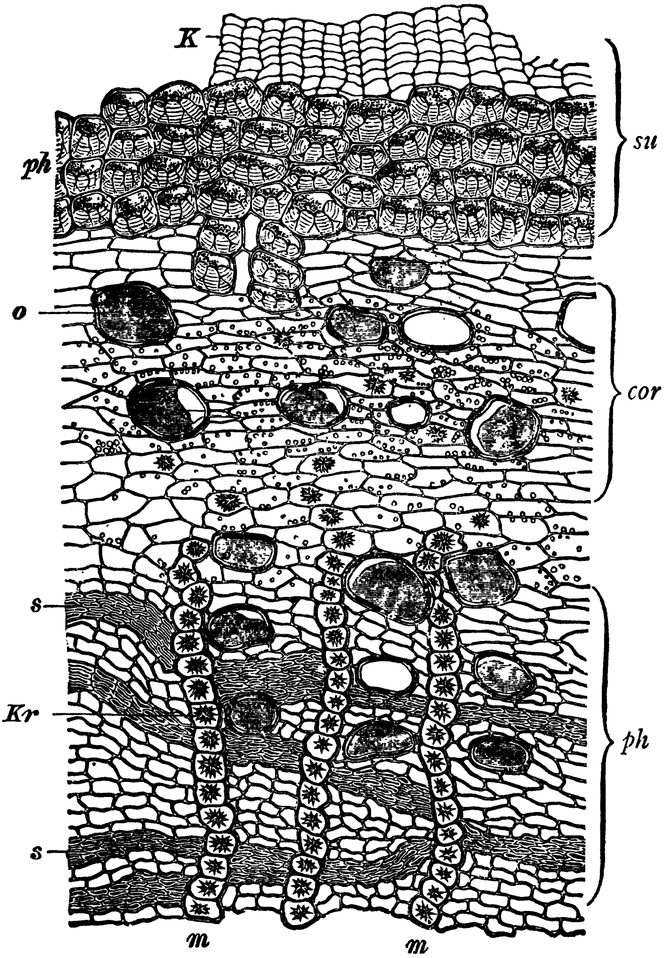


FIG. 235.—Canella: Transverse section of bark, showing tissues of outer bark (*su*); middle bark or cortical region (*cor*); and inner bark (*ph*). *K*, cork cells; *ph*, inner layer of periderm, the stone cells 40 to 90 microns in diameter with strongly thickened, distinctly lamellated, porous and lignified inner walls; *o*, large oil cells with yellowish content, scattered in starch-bearing parenchyma, the starch mostly single grains, 5 to 20 microns in diameter; *s*, collapsed cells of sieve; *m*, medullary rays mostly one cell wide, each cell with a rosette of calcium oxalate (*Kr*) up to 50 microns in diameter. (After Tschirch.)

Canella, Canella Bark or White Cinnamon (U. S. P. 1820 to 1882; N. F. 1916 to 1936) is the bark of *Canella alba*, a small evergreen tree indigenous to the West Indies and Florida. When bark is collected the light grayish cork is removed, the periderm of stone cells remaining. Bark in quills or curved pieces;

from 1.5 to 5 mm. in thickness; light yellowish brown to orange brown; somewhat scaly, reticulately wrinkled and fissured; fracture short, granular, with numerous secretion cells and wavy medullary rays; odor cinnamon-like; taste aromatic, pungent, somewhat bitter.

The structure is shown in Figure 235.

Canella bark contains mannitol, resin and 0.5 to 1.28 per cent of a volatile oil containing eugenol, cineol, caryophyllene and pinene. Total ash 6.35 per cent; acid-insoluble ash 0.15 per cent.

Canella is an aromatic and is used as a stimulant. It is also a condiment.

The barks of one or more species of *Cinnamodendron* of tropical America are sometimes substituted for canella bark, but they are distinguished by containing tannin, which is not found in canella.

Powder of Aloes and Canella or Hiera Picra (U. S. P. 1820 to 1882; N. F. 1888 to 1936) is a mixture of Aloes, 4 parts, and Canella, 1 part, reduced to a fine powder. The carminative action of the canella modifies the purgative action of the aloes.

TURNERACEÆ, OR DAMIANA FAMILY

This is a small family of tropical plants, of which there are about 6 genera and 100 species, distinguished among other characteristics by the fact that they contain tannin cells in the primary cortex, which are frequently developed in the form of idioblasts. In the pericycle occur isolated groups of bast fibers. Glandular and non-glandular hairs of a number of types are developed. Large nectarial glands occur on the margin and base of the leaves of *Turnera* and other genera.

Damiana or Turnera (N. F. 1916 to 1942) is the dried leaf of *Turnera diffusa* or of *Turnera aphrodisiaca*. The plant is a shrub growing in Brazil, Bolivia, Mexico, the West Indies and California. Most of the commercial supply comes from La Paz, Bolivia.

Description and Structure.—See Figure 236 and the National Formulary, Seventh Edition.

Powder.—Yellowish green; non-glandular hairs numerous, from 500 to 900 microns in length and from 20 to 30 microns in width, having at the base small lumina and often being curved toward the surface of the stem or leaf; fragments of the stem epidermis with rectangular cells and a few broadly elliptical stomata; subepidermal cells with lignified walls; tracheæ, small, spiral or having bordered pores; tracheids strongly lignified; thick-walled sclerenchyma, few; leaf epidermal cells with somewhat wavy walls and associated with stomata attaining a length of 30 microns, the stoma cells usually containing green plastids; numerous crystals of calcium oxalate mostly in rosettes from 15 to 30 microns in diameter, occasionally in prisms; few simple starch grains up to 12 microns in diameter.

Damiana contains volatile oil, less than 1 per cent; a non-glucosidal bitter principle; a hard brown resin; a mixture of soft resin and chlorophyll; tannic acid; a gummy substance; and protein substances, nearly 15 per cent. Total ash, about 7.5 per cent; acid-insoluble ash, about 2 per cent.

Damiana contains not more than 15 per cent of the stems of the plant and yields not more than 4 per cent of acid-insoluble ash.

The drug is a stimulant and a laxative, with some reputation as an aphrodisiac. Average dose, 2 gm.

VIOLACEÆ, OR VIOLET FAMILY

Viola or Violet (U. S. P. 1820 to 1882) is the dried flowering plant of *Viola pedata* Linné. Bird's-foot Violet is indigenous in eastern United States west to the Mississippi River. It is an herbaceous perennial up to 30 cm. high with a short thick rhizome, single flowers on scapes and radical, deeply cut leaves.

Viola Tricolor or Pansy (U. S. P. 1882 to 1894) is the wild-grown flowering herb of *Viola tricolor* Linné. Violet plants contain an alkaloid with a mild action like that of emetine causing nausea, purging and prostration in dogs. The drug, especially in Europe (*Viola odorata*), has long had repute as a remedy in infantile convulsions, dysentery, catarrhs and in cutaneous diseases.

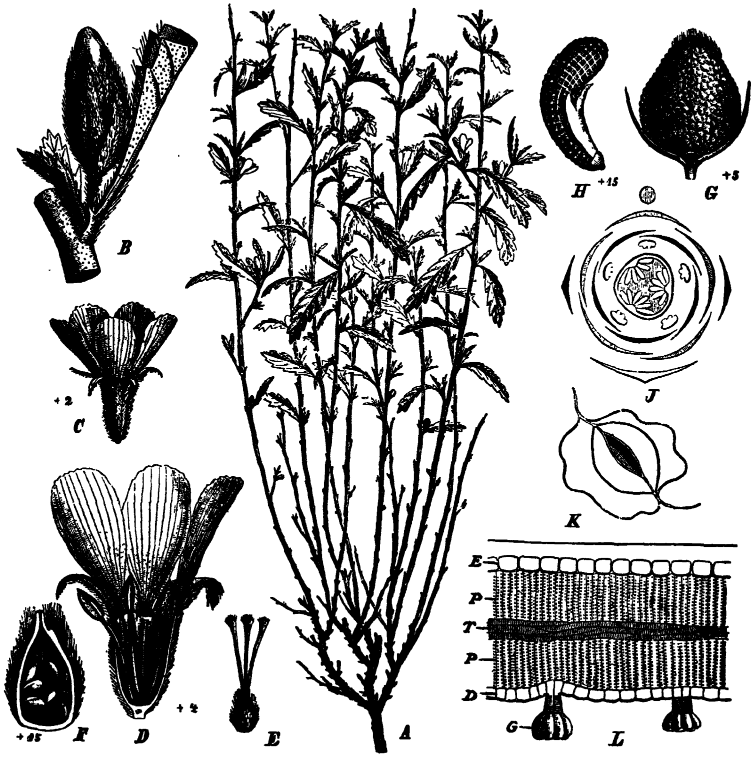


FIG. 236.—*Turnera aphrodisiaca:* *A*, portion of the plant showing the small serrate leaves. *B*, Portion of twig showing the flower bud. *C* and *D*, The flowers, the latter being in longitudinal section. *E*, Ovary with three long styles. *F*, Longitudinal section through the ovary showing a number of the ovules. *G*, The mature ovoid fruit. *H*, A cresent-shaped, reticulate seed, having a small, thin, membranous arillus. *K*, Stoma with subsidiary cells parallel to the pore. *L*, Transverse section through the leaf, showing upper epidermis (*e*); lower epidermis (*d*) with 2 glandular hairs (*g*); palisade cells (*P*); and tracheæ (*T*). *J*, Diagrammatic section of a flower of *T. ulmifolio.* (*B* and *J* after Urban; the remainder after Gilg.)

PASSIFLORACEÆ, OR PASSION FLOWER FAMILY

The plants of this family are mostly herbaceous or woody vines, and represented by about 18 genera and 325 species. They are most abundant in South America, a few of the species of *Passiflora*, however, being quite common in the southern United States. Nearly all of the plants have elongated tannin sacs and intercellular secretory canals, with a brownish content. Non-glandular hairs are either unicellular or uniseriate, the former usually having a more or less hooked summit. Glandular hairs are usually of a woolly or shaggy type. Large nectarial glands are common to a number of the species. In the leaves, the epidermal layer is frequently modified to mucilage and occasionally is papillose; the cells of the mesophyll may contain spicular cells or crystal idioblasts.

Passiflora, Wild Passion Flower or Passion Vine (N. F. 1916 to 1936) is the dried flowering and fruiting top of *Passiflora incarnata*, a perennial climbing herb, producing axillary tendrils, having alternate palmately lobed leaves and large showy flowers, which are supposed to typify the passion of Jesus and thus gave rise to the popular name given to this plant by the early Spanish settlers as well as the botanical name. The plants are indigenous to the southern United States, being found as far west as Missouri and Texas. They produce an abundance of flowers from May to July. The drug is usually collected after some of the berry-like fruits have developed, and is carefully dried and preserved. Leaves more or less broken, when entire, 3- to 5-cleft, long petiolate, the lobes lanceolate-ovate, apex acute, margin serrate; light greenish brown to dark purplish brown, somewhat coriaceous, and either glabrous or slightly pubescent. Flowers solitary, on long peduncles, from 2 to 5 cm. in breadth, the 5 sepals slightly united at the base and having at the crown several rows of purplish filaments, known as the corona; petals 4 to 5, inserted on the calyx and of a yellowish white color; stamens 5, monadelphous; ovary superior, unilocular, becoming in fruit a berry, from 4 to 5 cm. in length, having 3 to 4 parietal placentæ, and numerous ovoid, flattened seeds having a yellowish or brown aril. The drug has a slight odor and a somewhat acrid taste.

Passiflora may contain an alkaloid in small percentage.

Allied Drugs.—The rhizome and roots of *Passiflora incarnata* and *P. lutea* are sometimes used in medicine. They occur in cylindrical pieces from 3 to 6 mm. in diameter, light yellowish brown and finely striate. The leaves alone are sometimes collected, and a preparation is sometimes made from the freshly expressed juice of the plant.

CARICACEÆ, OR PAPAW FAMILY

This is a family composed of 2 genera of latex-containing trees, growing in tropical America, the best known of which is the genus *Carica*. The latex occurs as a finely granular protoplasm-like substance, which contains the peptonizing ferment papain, in articulated laticiferous tubes, which occur in the pith, cortex and xylem of roots and stems and are associated with the vascular bundles in leaves, even penetrating into the mesophyll. The pericycle is composed of isolated groups of bast fibers. The tracheæ are marked by simple pores or reticulate and scalariform thickenings. The medullary rays and wood fibers are apparently replaced with parenchyma.

PAPAIN

Papain (N. F. 1947 to date) is the dried and purified latex of the fruit of *Carica Papaya* Linné. Papain possesses a digestive activity not less than that of Reference Papain. The tree is indigenous to tropical America and is cultivated in Ceylon, Tanganyika, Hawaii, Cuba, Florida and other parts of tropical America. It is up to 5 meters in height and about 15 cm. in diameter. It has an active life of about five years. The pistillate flowers are about 2.5 cm. in length, 1 to 3 in short-stalked cymes, at the base of the leaf stalks. The fruit, in the tropics, may attain a length of 30 cm. and a weight of 5 kg. The epicarp adheres to the orange colored, fleshy sarcocarp which surrounds the central cavity containing a mass of nearly black seeds.

The full-grown, unripe fruit receives shallow incisions once a week on four sides of the fruit. The latex flows freely for a few seconds and then stops, after which it is collected and soon coagulates into lumps. Collections are made between 5 and 10 A.M. The lumps are shredded and dried in the sun or by means of artificial heat, the latter method yielding the better grade of crude papain. It is purified by dissolving in water and precipitating with alcohol.

DESCRIPTION AND ASSAY.—See the National Formulary.

CONSTITUENTS.—Papain contains several enzymes: one or more proteolytic enzymes; a coagulating rennet-like enzyme which acts upon the casein of milk; an amylolytic enzyme; a clotting enzyme similar to pectase; and an enzyme having a feeble action on fats. It is quite apparent that more than one proteolytic enzyme is present, because a single sample of papain will yield variable results depending upon the protein used in the substrate. The best grade will digest 300 times its weight of egg albumen.

USES.—Papain is used as a digestant for proteins, having an action similar to pepsin. In the meat packing industry it is extensively used for tenderizing ham.

CACTACEÆ, OR CACTUS FAMILY

This is a remarkable family of about 1500 species of succulent plants, growing largely in the arid regions of Mexico, Brazil and other parts of America. They usually possess thick, fleshy stems, the structure of which is adapted to a desert climate, the foliage leaves being modified to thorns. Mucilage cells and lysigenous canals are common to all of the plants of this family. In addition there are crystal cells and laticiferous canals. Calcium oxalate is excreted in enormous quantities, sometimes being present to the extent of 85 per cent of the ash of the plant. It occurs in the form of large rosettes, raphides, octahedra, tetragonal and monoclinic prisms. Sometimes they occur as sphæro-crystals and may resemble half-compound starch grains in the arrangement of their needle-like crystals. Occasionally the crystals are contained in idioblasts. In alcoholic material sphæro-aggregates may crystallize out in some of the cells. In *Epiphyllum,* curiously shaped protein bodies are distributed. The guard cells of the stomata are accompanied on both sides by one or more subsidiary cells parallel to the pore. The thorns are variously interpreted as being foliar organs, emergencies, *i. e.,* multicellular hairs derived from both the epidermal and hypodermal layers, or transitions between leaf-prickles and trichome-prickles. The tracheæ possess either simple pores or spiral thickenings; the wood fibers usually have simple pores; and the medullary ray cells may become lignified. In addition, tracheid-like parenchymatous cells are found in the wood of *Opuntia* and other genera.

Cactus Grandiflorus or Night-blooming Cereus (N. F. 1916 to 1947) is the fresh succulent stem of the wild-growing *Selenicereus grandiflorus* (Linné) Britton et Rose. The plant is a perennial with thick succulent stems and large fragrant flowers, expanding only at night and lasting but a few hours. It is

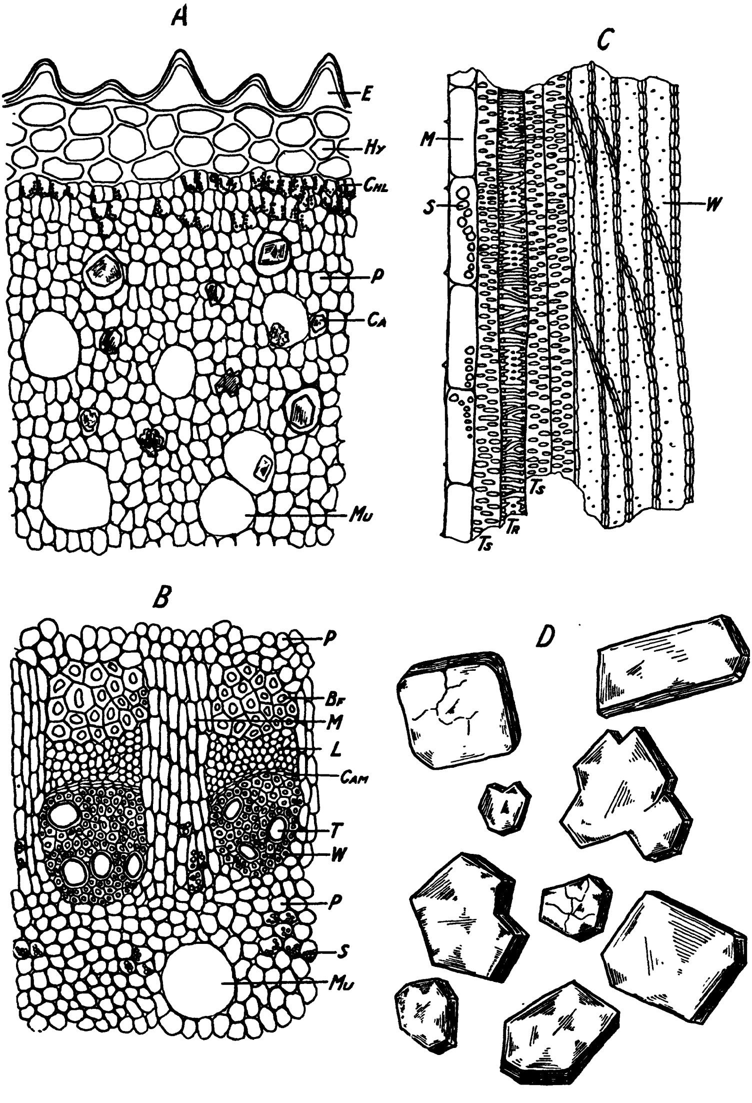


Fig. 237.—Cactus. Grandiflorus, *A*, section of stem: *E*, papillose epidermis; *Hy*, hypodermis; *P*, cortical parenchyma containing chloroplasts (*Chl*); *Ca*, solitary crystals of calcium oxalate up to 400 microns in length; *Mu*, mucilage cells. *B*, Transverse section of the fibrovascular bundles: *Bf*, bast fibers; *M*, broad medullary rays, the cells containing starch; *L*, leptome; *Cam*, cambium layer; *T*, tracheæ; *W*, wood fibers; *P*, starch-bearing parenchyma (*S*), the grains up to 10 microns in diameter; *Mu*, mucilage cell. *C*, Longitudinal section of xylem portion of bundle: *M*, parenchymatous cells containing starch (*S*); *Ts*, tracheæ with large simple pores; *Tr*, reticulate tracheæ; *W*, wood fibers. *D*, Solitary crystals of calcium oxalate. (Drawing by Haase.)

indigenous only to the West Indies, though it is extensively cultivated as a house plant. Commercial supplies have come largely from Mexico, collected from a variety of cactus plants, and without therapeutic value. The drug is shipped preserved in alcohol which is then used to extract it.

The drug consists of cylindrical, five- to nine-angled, branching, stems; 1 to 4.5 cm. in thickness; externally bright green and with alternate clusters of nine to twelve acicular spines about 5 mm. in length and as many bristles about 1 cm. in length; internally bright green, having a thick cortex with large mucilage cells and a small central woody cylinder. For the structure, see Figure 237.

The drug contains a glucoside, one or more resinous substances, and possibly an alkaloid.

Cactus Grandiflorus has been used as a substitute for digitalis. Only the best West Indian drug should be employed. Average dose, 0.5 gm.

Mescal Buttons or Anhalonium are the dried tops of several species of **Lophophora** growing in northern Mexico. The main axis of the plant is under ground, and from it arise a number of aerial shoots, which are more or less button-shaped or disk-like, being about 20 to 50 mm. in diameter. In the center of the disk occur tufts of hairs and usually one or more pinkish flowers. The drug contains several alkaloids, including mescaline, to which most of the symptoms of mescal poisoning, including the magnificent color vision, is due. Alkaloidal principles are also found in other members of the *Cactaceæ*.

THYMELEACEÆ, OR MEZEREON FAMILY

This is a family of about 40 genera and 500 species of shrubs and trees, most abundant in Australia and South Africa, a few of the genera, however, being found in the United States. The plants have simple, deciduous or evergreen leaves and small, mostly perfect flowers; and the fruits are usually berry-like drupes. Calcium oxalate is secreted in many forms. The plants possess no internal secretory cells or glandular hairs. The non-glandular hairs are usually unicellular. In the leaves there is mucilaginous metamorphosis of the epidermal cells, the latter often becoming papillose. The stomata usually occur only upon the upper or ventral surface of the leaf and are frequently enclosed in receptacles formed by the papillose elevations of the neighboring cells.

MEZEREUM

Mezereum or Mezereon (U. S. P. 1820 to 1926; N. F. 1926 to date) is the dried bark of *Daphne Mezereum* Linné, of *Daphne Gnidium* Linné, or of *Daphne Laureola* Linné. Daphne was a Greek nymph who was transformed into a laurel bush while fleeing from Apollo; *Gnidium* is an ancient name for laurel; *Laureola* means *laurel-like; mezereum* is from *mazariyum,* the Persian name of the plant. The plant is a slow growing deciduous shrub. The bark is collected in early spring; dried and frequently made up into small bundles, the commercial supplies being obtained from Thuringia, southern France and Algeria. Mezereum was used in English medieval times. It seems to have entered American practice through traditional English authority.

Description.—In flexible, tough quills or somewhat flattened strips; bark from 0.3 to 1 mm. in thickness; outer surface olive-brown, purplish brown or purplish gray, smooth, numerous lenticels, giving a transversely striated appearance and occasionally with numerous circular brownish black apothecia; inner surface pale yellow, satiny lustrous, finely striate; fracture tough, fibrous, the inner bark lamellated.

STRUCTURE.—Cork 20 to 40 rows, the outer compressed, the inner with tabular cells with nearly colorless walls; a hypodermis of 3 to 5 rows of collenchyma containing chloroplasts or a greenish yellow resinous substance; inner bark of loosely united groups of colorless bast fibers and sieve strands; medullary rays few, uniseriate.

POWDER.—Light brown; odor slight; sternutatory; taste slowly developing to strongly pungent and acrid; bast fibers up to 3 mm. in length and about 15 microns wide, more or less uneven or irregularly bent and attenuated at the ends, the walls colorless, non-lignified and free from pores; fragments of yellowish brown cork, and of medullary rays containing starch; starch grains relatively few, mostly spheroidal or ellipsoidal, and varying from 3 to 15 microns in diameter.

CONSTITUENTS.—An acrid resin known as mezerein; a crystalline, bitter glucoside, daphnin (isomeric with æsculin) occurring in greatest amount in the stem bark during the flowering and fruiting period; volatile and fixed oils; total ash, about 3.25 per cent; acid-insoluble ash, about 0.25 per cent.

USES AND DOSE.—Mezereum has been used as an alterative, a diuretic, a sialagogue and a stimulant. Average dose, 1 gm.

The berry-like fruits of *Daphne Mezereum* and *D. Gnidium* are subglobular, dark brown or brownish black, about 5 mm. in diameter, each with a black seed. The fruits are acrid and pungent and contain 0.38 per cent of coccogonin, a principle which on sublimation gives off an odor of coumarin; 0.22 per cent of an acrid resin; and 31 per cent of a fixed oil, which absorbs oxygen on exposure to air like a drying oil.

The barks of other plants of this family are used like mezereum, as *Daphnopsis schwartzii* of the West Indies, *Lasiosiphon eriocephalus* of India and Ceylon, and various species of *Stelleria*, *Struthiola* and *Thymelæa*.

Lasiosiphon meissnerianus (Fam. *Thymelaceæ*) is a shrub indigenous to South Africa, where the root is used as a cure for snake-bite. The chief constituent of the root is an amorphous, acrid resin, from which only a phytosterol, $C_{27}H_{46}O$, and a mixture of fatty acids could be obtained.

PUNICACEÆ, OR POMEGRANATE FAMILY

This is a small family represented by a single genus, *Punica,* of which there are two species. In the pericycle there are isolated groups of bast fibers, beneath which the cork develops. In the primary cortex occur large stone cells, either single or in small groups. The fibrovascular bundles are bi-collateral; bast fibers are wanting in the cortex; the tracheæ and wood fibers possess simple pores; and calcium oxalate is excreted in the form of rosettes.

GRANATUM

Pomegranate Fruit or Granatum (U. S. P. 1820 to 1842).
Pomegranate Fruit Rind or Granati Fructus Cortex (U. S. P. 1842 to 1882).
Pomegranate Bark or Granati Cortex (U. S. P. 1831 to 1842).
Pomegranate Root Bark or Granati Radicis Cortex (U. S. P. 1842 to 1882).
Pomegranate Root and Stem Bark or Granatum (U. S. P. 1882 to 1936).
Pelletierine Tannate (U. S. P. 1905 to 1947; N. F. 1947 to date).

All are derived from *Punica granatum* Linné, a shrub indigenous to northwestern India and cultivated in subtropical regions throughout the world for its edible fruit. All parts of the plant contain tannin (a mixture of two or more kinds); pomegranate rind, up to 28 per cent of tannin; the dried root bark, up to 22 per cent; hence these are very astringent drugs. The pulp of the fruit is used medicinally as an acidulous refrigerant. The stem and root barks have long been used as an anthelmintic and tænifuge; Dioscorides mentions a decoction of the root for the expulsion of tapeworm. The anthelmintic constituent, pelletierine, was discovered in 1878 and was found to be a mixture of four alkaloids.

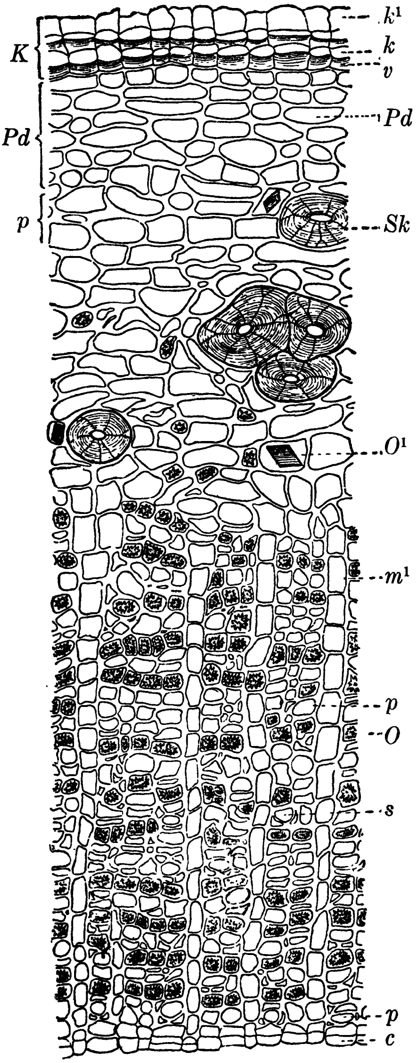


FIG. 238.—Transverse section of Granatum: *K*, corky layer composed of thin-walled cork cells (k^1) and thick-walled cork cells (*k*), only the inner walls (*v*) of which are thickened; *Pd*, phelloderm cells; *p*, a few parenchyma cells of the primary cortex; *Sk*, stone cells with thick, lamellated walls and fine, branching pores; *O*, rosettes of calcium oxalate; O^1, monoclinic prisms of calcium oxalate; m^1, medullary rays; *s*, sieve cells; *p*, parenchyma cells; *c*, cambium. (After Meyer.)

The dried fruit rind occurs in irregularly curved, yellowish brown fragments about 2 mm. in thickness. It assumes a bluish black color with ferric salts.

The dried scraped root bark is dark brown, with patches and scales of cork, no green phelloderm layer, and medullary rays extending nearly to the outer surface. The yield of pelletierine may be as high as 3 per cent.

The dried stem bark is in curved pieces or simple quills, the bark 0.5 to 3.5 mm. in thickness; the cork is dark gray, with lighter patches of foliaceous lichens with dark apothecia, yellowish brown lenticels, furrows and abraded patches; inner surface light yellow or light brown, finely striate or smooth; fracture short and even, the surface greenish in color. The structure of the stem bark is shown in Figure 238. It seldom yields more than 1.5 per cent of pelletierine.

The powdered barks are yellowish brown, with a slight odor and a marked astringency. The powder contains calcium oxalate rosettes and rhombohedra; numerous starch grains up to 10 microns in diameter; cork cells with strongly lignified walls; stone cells mostly single and up to 300 microns in length, the walls being very thick and strongly lamellated; tannin cells producing a deep blue color with solutions of ferric salts; wood fibers and tracheæ rare.

Pelletierine Tannate is a mixture in varying proportions of the tannates of the several alkaloids obtained from pomegranate. It contains an amount of the alkaloids equivalent to not less than 20 per cent as the hydrochloride.

The ground bark is mixed with lime and extracted with chloroform. After conversion of the alkaloids to sulfate and solution in water, they are precipitated as tannate by the addition of tannic acid. Four alkaloids are present: pelletierine (punicine), the most important, is colorless, volatile and liquid, with levorotatory salts; isopelletierine, optically inactive; methylpelletierine with dextrorotatory salts; pseudopelletierine (methylgranatonine), in prisms and optically inactive.

Average dose of pelletierine tannate, 0.25 gm.

MYRTACEÆ, OR MYRTLE FAMILY

This is a family of about 73 genera and 2750 species. They are shrubs and trees, chiefly indigenous to Australia and tropical America. The plants yield a large number of economic products, and some, as the *Eucalyptus,* are to be classed among the leading timber trees of the world. The leaves are simple, the flowers are perfect, and the fruits are either fleshy and berry-like or capsular. In certain species of *Eucalyptus* the leaves are both horizontal and vertical, the former being bifacial; the latter centric, with a twist in its short petiole. Schizogenous excretory cavities are characteristic of this family, and are distributed throughout the parenchyma of the stems and leaves, giving to the latter pellucid-punctate areas. The secretory cavities arise very early in the development of the tissues and the secretion, which is of an oily nature, develops in a resinogenous layer lining the cavity, the walls of which finally become more or less suberized. The inner bark usually consists of alternating layers of bast fibers and sieve. The non-glandular hairs are usually unicellular, and glandular hairs are wanting.

EUCALYPTUS

Eucalyptus (U. S. P. 1882 to 1936) is the dried, scythe-shaped leaf of *Eucalyptus Globulus.* This tree is indigenous to eastern Australia and Tasmania, and cultivated in southern Europe and southern United States, especially California. *Eucalyptus* is from the Greek meaning "well covered," alluding to the lid-like cover of the buds, and *globulus* (Latin) refers to the form of the fruit. The commercial supply of the drug is largely from southern France. The tree requires much water and has been used for drying up marsh land.

The leaves are up to 30 cm. long and 7.5 cm. wide, coriaceous and with a revolute margin; leaf surfaces grayish green, glabrous, pellucid-punctate, with numerous small circular, reddish brown dots of cork; odor slightly aromatic; taste aromatic, somewhat bitter and cooling.

The epidermal cells are polygonal with straight walls and have a thick cuticle covered with wax; sunken stomata are found on both surfaces; the mesophyll consists mostly of palisade cells beneath each epidermis, among which are distributed large, spheroidal oil-secretion cavities with a yellow oily content; rosettes or single prisms of calcium oxalate are found in cells of the central loose mesophyll.

The drug contains volatile oil, 3 to 6 per cent, of which up to 80 per cent is eucalyptol (cineol), the remainder consisting of *d*-pinene (eucalyptene) and other terpenes; several resins; a neutral bitter principle; eucalyptic acid and tannic acid. Total ash, 5.25 per cent; acid-insoluble ash, about 0.2 per cent.

Eucalyptus Kino, Australian Kino or Red Gum (N. F. 1926 to 1936) is the astringent exudation from *Eucalyptus rostrata* and other species of *Eucalyptus.* It occurs in masses or small fragments, which are of a ruby- or garnet-red color (not reddish black), somewhat dusty, but not so brittle as Malabar kino and contains 40 to 50 per cent of tannic acid; also kino red and catechin. From 80 to 90 per cent is soluble in cold water, the solution having a neutral reaction. Australian kino seems to be more unstable than Malabar kino and is converted into the insoluble kino red, particularly if not thoroughly dried. It is used as an astringent.

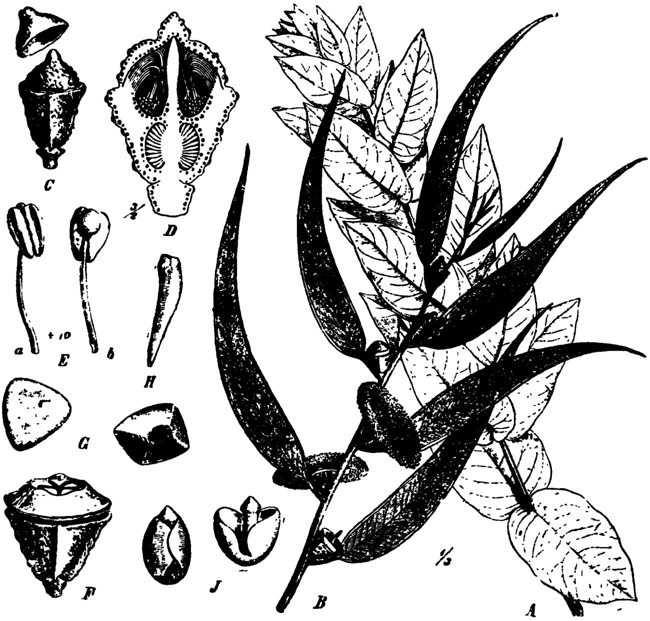


FIG. 239.—*Eucalyptus globulus: A*, young branch with opposite, oblong, dorsiventrall sessile leaves. *B*, Flowering branch with scythe-shaped, petiolate, scattered, bilatera, leaves. *C*, Flower-bud showing the detached upper portion of the perianth (operculum or lid) which covers the stamens until they are fully mature. *D*, Longitudinal section of a flower-bud showing incurved filaments which curve outward when the flower matures. *E*, Stamens in two views. *F*, Truncated capsule or pyxis. *G*, Two fertile seeds. *H*, Sterile seed, seeds of this kind usually being most numerous. *J*, Two germinating plants. (*A* to *F*, after Niedenzu; *G* to *J*, after Müller.)

Eucalyptus kino is also obtained from the following species: Iron-bark tree (*E. leucoxylon*), *E. gunnii*, *E. obliqua*, *E. piperata*, *E. ficifolia*, *E. stellulata*, *E. macrorhyncha*, *E. amygdalina radiata.* So-called Botany Bay kino was at one time supposed to be obtained from *Eucalyptus resinifera.*

Eucalyptus Oil (U. S. P. 1882 to date) is the volatile oil distilled with steam from the fresh leaves of *Eucalyptus globulus* Labillardiere, or from other species of *Eucalyptus.* The oil is a colorless or pale yellow liquid, having a characteristic, aromatic, somewhat camphoraceous odor, and a pungent, spicy cooling taste. Consult the U. S. Pharmacopœia for its constants.

Standards.—Eucalyptus oil contains not less than 70 per cent of eucalyptol, which is determined by the freezing point, not below −15.4° C. Eucalyptus oil must be free from heavy metals and from eucalyptus oils containing large amounts of phellandrene.

Uses and Dose.—Eucalyptus oil is an antiseptic and antiperiodic, a diaphoretic and an expectorant. Average dose, 0.5 cc.

Some thirty species of Eucalyptus yield oils containing phellandrene; many others yield oils containing less than 70 per cent of eucalyptol, though phellandrine may be absent. Both of these types have been admixed with the official oil.

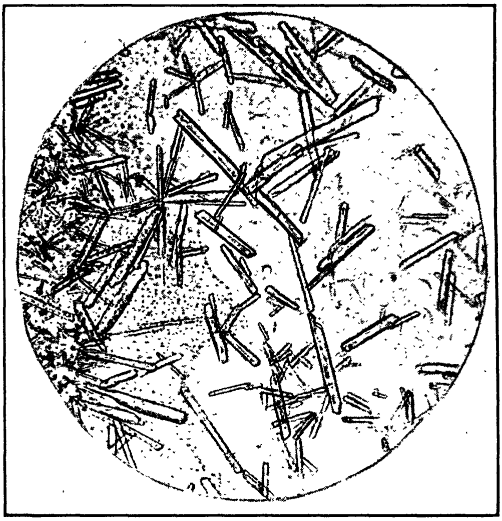


Fig. 240.—Crystals obtained by treating eucalyptol with 5 per cent hydroquinone solution.

Eucalyptol or Cineol (U. S. P. 1894 to date) is obtained from eucalyptus oil and from other sources. It is a colorless liquid having a characteristic, aromatic, camphoraceous odor and a pungent, cooling spicy taste. The oxygen atom in eucalyptol apparently does not possess alcoholic, ketonic, aldehydic or acid properties. Eucalyptol may be obtained (1) from eucalyptus oils by fractional distillation and subsequent freezing of the distillate or by treating eucalyptus oil with phosphoric acid and subsequently decomposing the eucalyptol-phosphoric acid with water; or (2) it may be obtained as a dehydration product of terpin hydrate on treatment with acids.

Eucalyptol is optically inactive and should be free from oil of eucalyptus and phenols. Consult the U. S. Pharmacopœia for its constants.

Microchemistry of Eucalyptol.—When a drop of eucalyptol (or a drop of oil of eucalyptus or a few drops of an alcoholic extract of eucalyptus leaf) is treated with a drop of a 5 per cent solution of hydroquinone on a slide, colorless prisms and rhomboids occur (see Fig. 240); with a 50 per cent solution of resorcinol, leaf-like crystals are formed; bromine vapors cause reddish yellow, branching crystals.

Uses and Dose.—Eucalyptol has properties similar to those of eucalyptus oil. Average dose, 0.3 cc.

Cajuputi or Cajuput Oil (U. S. P. 1820 to 1936) is the volatile oil
om the fresh leaves and twigs of several varieties of *Melaleuca leuca-*
d rectified by steam distillation. The plants are found in the Philip-
East Indies and Australia. Oil of cajuput contains from 50 to 65 per
alyptol (cajuputol), terpineol and various terpenes. It is used exter-
arasiticide and internally as a carminative, stimulant and diaphoretic.

Other volatile oils containing eucalyptol include oils of lavender, levant wormseed, rosemary, sage, ginger, canella and cardamom.

CLOVE

Clove or Cloves (U. S. P. 1820 to date) is the dried flower bud of *Eugenia caryophyllata* Thunberg. *Eugenia* (Latin) and *caryophyllata* (Greek) mean "nut-leaf," and refer to the nut-like flower buds; "clove," from the Latin *clavus*, a nail, refers to the shape of the whole spice.

The plant is a tree up to 15 meters in height indigenous to the Molucca Islands but cultivated in Penang, Amboyna, Zanzibar, Sumatra, Madagascar, Seychelles, Mauritius and the West Indies: the buds are gathered when they change in color from green to crimson and are carefully dried in the sun. The best cloves come from Penang. Clove was known to the Chinese before 266 B.C. The Dutch, who won possession of the Spice Islands in 1605, endeavored to create a monopoly and destroyed all of the trees except those on the islands of Amboyna and Lernate. In 1770, however, the French succeeded in introducing the tree into Mauritius and the Isle of Bourbon from where its cultivation spread to other clove-growing areas.

DESCRIPTION, STRUCTURE AND POWDER.—See Figure 241 and the U. S. Pharmacopœia.

CONSTITUENTS.—Clove contains a volatile oil, 14 to 20 per cent; gallotannic acid, 10 to 13 per cent; caryophyllin, white, odorless, tasteless, crystallizing in silky needles; vanillin; eugenin; total ash, 6.15 per cent.

STANDARDS.—Clove yields, from each 100 gm., not less than 16 cc. of clove oil; not more than 10 gm. of crude fiber; and not more than 0.75 gm. of acid-insoluble ash. Contains not more than 5 per cent of its stems and not more than 1 per cent of other foreign matter.

USES AND DOSE.—Clove is a stimulant, a carminative and an aromatic. Average dose, 0.25 gm.

Clove Stems are subcylindrical, jointed, sometimes branching, brown, and less aromatic than clove, yielding from 4 to 7 per cent of volatile oil.

Clove Fruit (Mother of Cloves) is the nearly ripe fruit of the clove tree. It is about 2.5 cm. long, 10 mm. thick, ovoid, brown, 2- to 4-seeded and only slightly aromatic. Clove stem may be detected in powdered clove, by irregular or polygonal stone cells up to 70 microns in diameter, with thick porous walls and large lumina frequently filled with a yellowish brown amorphous substance; clove fruits contain starch. It is stated that artificial clove has been made by using starch, gum and oil of clove; or from dough and clove powder. This is easily distinguished by adding the spurious article to water, when the compound disintegrates. Clove partially exhausted by steaming off a portion of the volatile oil is also used as an adulterant of clove. Partially exhausted clove is a by-product of the pickling industry and this is sometimes offered for the genuine.

Clove Oil or Oil of Cloves (U. S. P. 1820 to date; as clearing agent, U. S. P. 1916 to 1926; N. F. 1926 to date) is the volatile oil distilled with steam from the dried flower buds of *Eugenia carophyllata* Thunberg, and contains not less than 82 per cent by volume of eugenol.

DESCRIPTION.—It is a colorless or pale yellow liquid, becoming darker and thicker by age or exposure to air, and having the characteristic odor and taste of clove. For solubilities and constants consult the U. S. Pharmacopœia.

CONSTITUENTS.—The oil contains eugenol, acetyleugenol, the sesquiterpenes *a*- and *b*-caryophyllene, small quantities of furfural, esters and ketones.

USES.—Oil of clove is a flavoring agent, a stimulant, aromatic, carminative and antiseptic. It is employed as a remedy in toothache. Oils with a high eugenol content are used for the production of vanillin (see page 188).

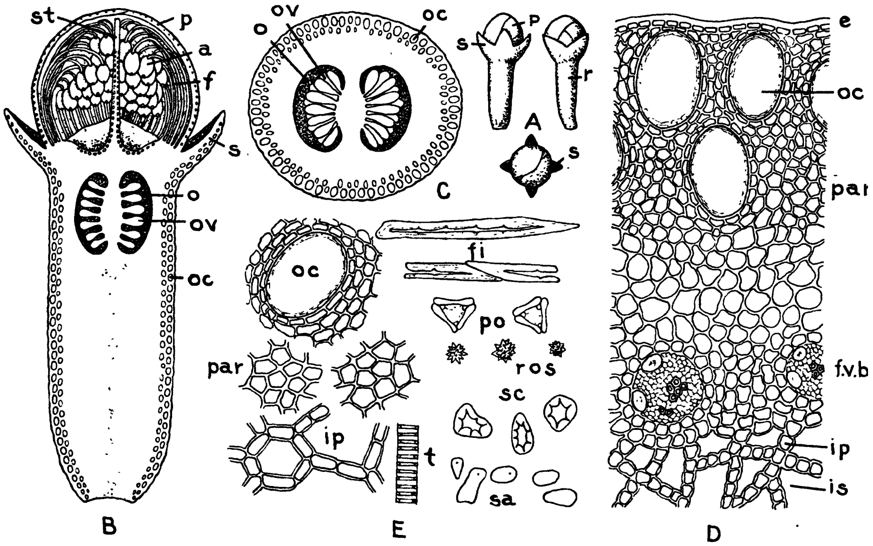


FIG. 241.—*Eugenia caryophyllata: A*, Entire flower buds in side and upper view showing the cylindrical receptacle (*r*), the four calyx teeth (*s*) and the globular closed corolla consisting of four petals (*p*). *B*, Longitudinal section through the flower-bud showing petals (*p*); anthers (*a*); filaments (*f*), style (*st*); ovary (*o*); ovules (*ov*) and oil cells (*oc*). *C*, Transverse section through the receptacle at the location of the ovary showing the bilocular ovary (*o*); the ovules (*ov*) and oil cells (*oc*). *D*, Transverse section through the outer portion of the receptacle showing epidermis (*e*); oil cells (*oc*), outer parenchyma (*par*) and inner parenchyma (*ip*) with large intercellular spaces (*is*) and fibrovascular bundles (*fvb*). *E*, Powdered clove showing oil cells (*oc*); fibers (*fi*); parenchyma (*par*) and inner parenchyma (*ip*); spiral tracheæ (*t*); pollen grains (*po*) from 15 to 20 microns in diameter; and rosettes of calcium oxalate (*ros*) from 10 to 15 microns in diameter. The drawing also shows stone cells (*sc*) from clove stem and starch grains (*sa*) from clove fruit. (Drawings by Harry Flower.)

Eugenol (U. S. P. 1905 to date) is a phenol, $C_{10}H_{12}O_2$, obtained from clove oil and from other sources. It is usually prepared from clove oil by shaking with a 10 per cent solution of sodium hydroxide to form sodium eugenolate. The mixture is washed with ether, and the sodium eugenolate then decomposed with sulfuric acid, and the eugenol separated by steam distillation. It is a colorless or pale yellow, thin liquid, having a strongly aromatic odor of clove and a pungent spicy taste. Consult the U. S. Pharmacopœia for its physical and chemical constants.

MICROCHEMISTRY OF EUGENOL.—A very satisfactory microchemical test for eugenol either in volatile oils or in drugs consists of placing a drop of the oil (or of a chloroformic extract of the drug) on a slide, adding a drop of 3 per cent aqueous solution of sodium hydroxide saturated with sodium bromide and covering with a cover glass. Almost immediately crystals of sodium eugenolate appear, which consist of needle and pear-like forms arranged in rosette-like bunches (see Fig. 242).

USES AND DOSE.—The properties of eugenol are similar to those of oil of cloves. Average dose, 0.1 cc.

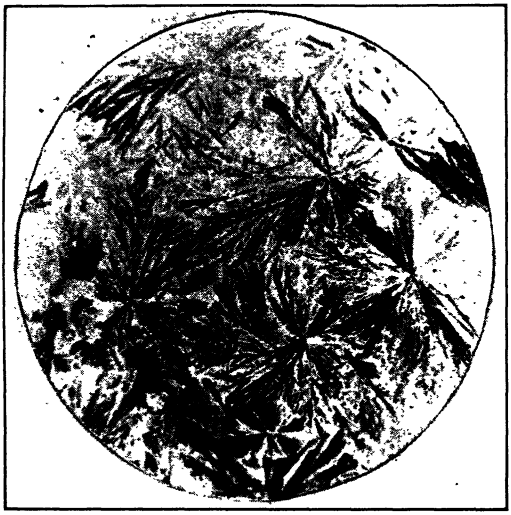


FIG. 242.—Crystals of sodium eugenolate.

PIMENTA

Pimenta or Allspice (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the dried nearly ripe fruit of *Pimenta officinalis*, a tree indigenous to the West Indies. Mexico, Central America and Venezuela, where it is also cultivated, especially in Jamaica. The full-grown but still green fruit is collected and dried in the sun.

Pimenta is subglobular, 4 to 7 mm. in diameter; externally dark brown, glandular-punctate; pedicel 4 to 6 mm. in length; pericarp about 1 mm. in thickness; internally light brown, 2-locular, 2-seeded, dissepiments thin; seed campylotropous, plano-convex, slightly reniform, about 4 mm. in length; externally reddish brown, smooth, shiny.

For the structure see Figure 243.

The powder is dark brown, aromatic, and exhibits rosette aggregates of calcium oxalate up to 20 microns in diameter; single or compound starch grains from 3 to 20 microns in diameter; stone cells large, nearly isodiametric, very thick-walled, with numerous simple pores and branched canals and nearly colorless contents; oil-secretion cavities with wine-colored contents; oil globules numerous; parenchymatous cells occasionally lignified, and with irregular reddish brown tannin masses; non-glandular hairs of the stem very few.

Allspice contains a volatile oil (3 to 4 per cent), consisting of about 65 to 80 per cent of eugenol; a resin; an acrid fixed oil, about 6 per cent; and tannic acid; total ash 4 per cent; acid-insoluble ash, 0.15 per cent.

Pimenta is a stimulant, a carminative and an aromatic flavoring agent.

Ground allspice has been adulterated with clove stems, cocoa shells, and the endocarp of the olive.

ALLIED PLANTS.—A variety of *P. officinalis* yields a fruit with larger drupes, known as **Tobasco or Mexican Allspice**. The structure of this fruit resembles that of pimenta, as does also the **Crown Allspice** obtained from *P. acris*, a tree of tropical America, the fruits of which are 8 to 10 mm. in length.

Pimenta Oil or Oil of Allspice (U. S. P. 1820 to 1926; N. F. 1926 to date) is a volatile oil distilled from the fruit of *Pimenta officinalis* Lindley, and yields not less than 65 per cent, by volume, of phenols calculated as eugenol.

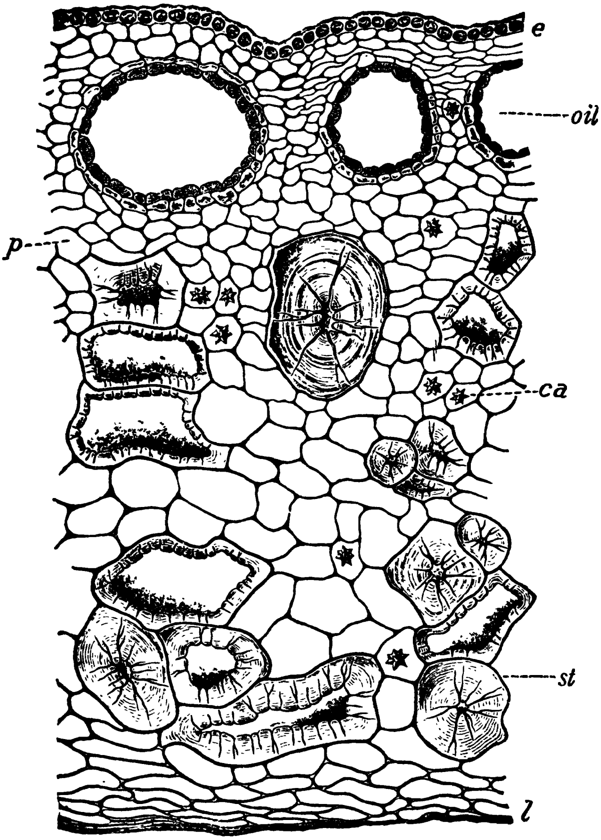


FIG. 243.—Pimenta: Outer wall of pericarp showing epidermal cells of epicarp (*e*); cells of mesocarp consisting of oil-secretory cavities (*oil*), stone cells (*st*) and parenchyma (*p*) containing rosette aggregates of calcium oxalate (*ca*); endocarp consisting of stone cells beneath which is a layer of more or less collapsed cells (*l*). (After Moeller.)

The oil is obtained by steam distillation. It is a colorless, yellow or reddish yellow liquid having the characteristic odor and taste of allspice. Consult the National Formulary for its physical and chemical constants.

CONSTITUENTS.—Oil of pimenta contains from 65 to 80 per cent of eugenol; caryophyllene; cineol; phellandrene and methyl eugenol.

USES AND DOSE.—Oil of pimenta is a stimulant, a carminative and an aromatic. Average dose, 0.1 cc.

Myrcia Oil or Oil of Bay (U. S. P. 1882 to 1905; N. F. 1916 to date) is a volatile oil distilled from the leaves of *Pimenta racemosa* (Miller) J. W. Moore, and yields not less than 50 per cent and not more than 65 per cent, by volume, of phenols.

The bay tree is a beautiful tree attaining the height of about 15 meters, growing in the West Indies. The leaves are distilled with steam to yield the oil, which is a yellow or brownish yellow liquid having a pleasant aromatic odor and a pungent spicy taste. Consult the National Formulary for its physical and chemical constants.

Constituents.—Myrcia oil contains from 55 to 65 per cent of eugenol; methyl eugenol; chavicol; methyl chavicol; phellandrene; citral and myrcene.

Uses.—Myrcia oil is extensively employed in the perfume industry. It is the principal constituent of Compound Myrica Spirit (Bay Rum).

Adulterants.—The leaves of two varieties of *P. acris*, known locally as "Bois d'Inde Citronelle" and "Bois d'Inde Anise," are frequently admixed with the leaves of the true Bay to the great detriment of the oil subsequently distilled. The oil from the "Citronella" variety (*P. acris* var. *citrifolia*) contains citral and has the flavor of lemon. Why the oil from the "Anise" variety does not reach the desired standard is not yet clear. The varietal forms intermingle in extensive wild growths near the coasts of many of the West Indian Islands and the leaves are gathered indiscriminately. Much harm has already resulted to the bay oil industry, and it is a matter of great concern to the distillers that either some method be determined for distinguishing the undesirable leaves or that plantations of the true *P. acris* be established.

ARALIACEÆ, OR GINSENG FAMILY

This family consists of about 50 genera and 500 species of plants which are widely distributed. They are perennial herbs, shrubs or trees. The leaves are mostly palmately lobed or compound; the flowers are small, perfect or polygamous, frequently occurring in umbels; the fruit is either a berry or a drupe. The plants possess schizogenous secretion canals in the parenchyma of pith, cortex and leaves. Sometimes the leaves are pellucid-punctate due to secretion cavities. In the root, resin canals are generally situated opposite the strands of xylem and phloem causing an exceptional displacement of the young lateral branches. The canals and cavities may contain volatile oil, resin, gum, and occasionally a milky content. In a number of species of *Aralia* collateral medullary vascular bundles are developed, which are inversely orientated, *i. e.*, the phloem is directed toward the center of the pith and the xylem in the direction of the cortex. Weiss has shown that these bundles in *Aralia racemosa* appear first as normal bundles in the peripheral ring and only enter the pith later, at the same time undergoing a rotation through 180 degrees. The leaves are usually glabrous, but in the floral parts both glandular and non-glandular hairs of several different forms occur.

ARALIA

Aralia, American Spikenard or Spignet (N. F. 1916 to date) consists of the dried rhizome and roots of *Aralia racemosa* Linné. The plant is a perennial herb growing in rich woodlands of the eastern United States and Canada to a height of 1 or 2 meters and possesses a thick, fleshy rhizome; large, ternately-compound leaves; and numerous umbels of small, greenish flowers, which are arranged in large compound panicles. The fruits are small, bright reddish or purplish drupes and give the plant a very handsome and striking appearance. The drug is gathered in the fall and sliced to facilitate drying. It should be very carefully dried and preserved.

DESCRIPTION.—Rhizome oblique, subcylindrical, more or less branched, 3 to 7 cm. in thickness; externally light brown, distinctly annulate, with numerous deeply concave stem scars from 2 to 3 cm. in width; numerous, somewhat fleshy roots, up to 2.5 cm. in diameter.

POWDER.—Light brown; aromatic; taste pungent and slightly acrid; starch grains numerous, single or 2- to 4-compound; calcium oxalate in rosette aggregates; tracheæ with simple pores or scalariform thickenings; sclerenchymatous fibers of pericycle with thick, strongly lignified, porous walls; characteristic lignified cells from the hypodermis, 40 to 100 microns in length and about one-half as broad, their walls showing simple pores.

CONSTITUENTS.—The drug contains a bitter and pungent volatile oil; resin; tannin; total ash, 5.49 per cent; acid-insoluble ash, about 0.55 per cent. The drug contains not more than 5 per cent of stem bases.

USES AND DOSE.—Aralia is a stimulant, an alterative and a diaphoretic. Average dose, 2 gm.

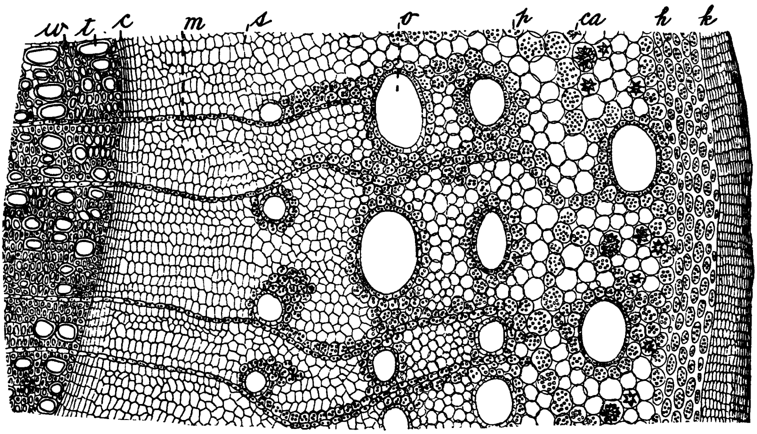


FIG. 244.—*Aralia nudicaulis:* Transverse section of rhizome showing cork (*k*), hypodermis (*h*), rosette aggregates (*ca*) of calcium oxalate, parenchyma (*p*) containing angular starch grains, oil-secretion canals (*o*), sieve (*s*), medullary rays (*m*), cambium (*c*), tracheæ (*t*), wood fibers (*w*).

Aralia Nudicaulis, American, Wild, or Virginian Sarsaparilla (U. S. P. 1820 to 1882) is the rhizome of *Aralia nudicaulis,* a nearly prostrate perennial herb, producing a very long rhizome, a solitary pinnately 3- to 5-foliate leaf and a naked scape with 2 to 7 umbels of green flowers. The specific name *nudicaulis* means "naked stem," in allusion to the scape and rhizome of the species. The plant is common in moist woodlands of the eastern United States and Canada.

The rhizome attains a length of many meters and is from 5 to 15 mm. in thickness; externally grayish brown, longitudinally wrinkled and somewhat annulate; fracture short; internally bark light brown, with numerous large oil-secretion canals; wood yellowish, distinctly radiate; pith spongy, whitish; odor and taste aromatic.

The structure is shown in Figure 244.

The constituents are like those of Aralia. Total ash, 5.8 per cent; acid-insoluble ash, 0.2 per cent.

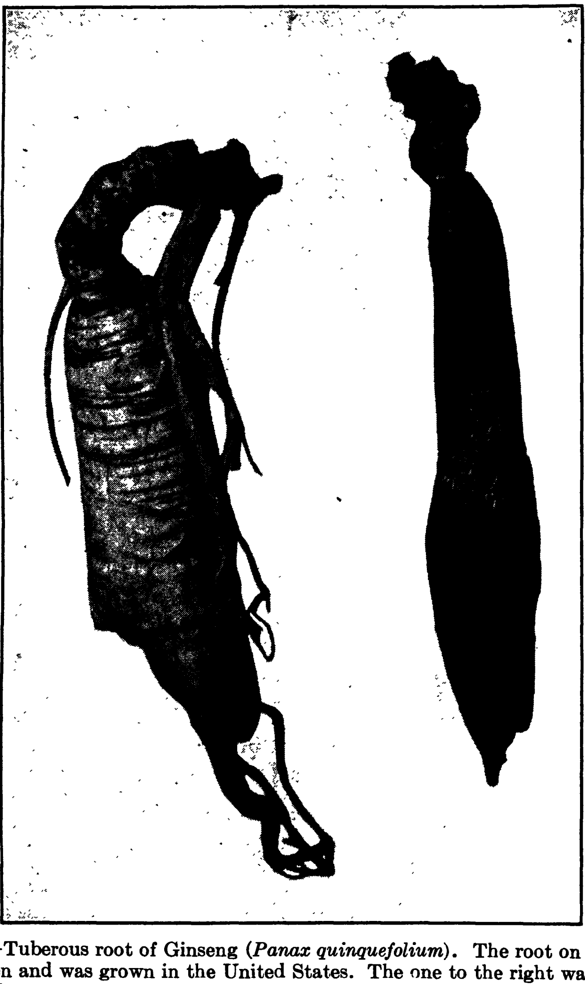


FIG. 245.—Tuberous root of Ginseng (*Panax quinquefolium*). The root on the left is a fresh specimen and was grown in the United States. The one to the right was purchased at a Chinese bazaar. It is translucent, of a yellowish brown color, and has the characteristic shape and markings considered desirable by the Chinese. The markings on the upper segment of the specimen are stem-scars which are usually found on old roots. The translucent appearance is no doubt due to the manner of treatment. While the method is not generally known, similar specimens may be prepared by treating the recently gathered roots with freshly slaked lime.

Aralia Nudicaulis has been used for the same purposes as Aralia. It is occasionally found as an adulterant of Aralia, but may be readily distinguished by the absence of characteristic hypodermal cells.

Aralia Spinosa, Prickly Elder, Angelica Tree or Hercules Club (U. S. P. 1820 to 1882) is the bark of *Aralia spinosa*, a shrub or tree growing on the banks of streams in the eastern United States.

It occurs in quills, or transversely curved pieces, bark 1 to 3 mm. in thickness; externally grayish brown, nearly smooth or irregularly wrinkled and having numerous lenticels; inner surface light yellowish brown, finely reticulate; fracture short-fibrous; outer portion of thin, easily separable dark brown cork and yellowish white cortex; odor aromatic; taste bitter and acrid.

The drug contains a volatile oil having a greenish yellow color; an acrid resin; a saponin (araliin); a tasteless resin; a crystalline substance; mucilage and chlorophyll. The drug contains neither tannic acid nor an alkaloid.

Aralia Spinosa is a stimulant and a diaphoretic.

It is often found as an adulterant of northern prickly ash bark.

Ginseng, Radix Ginseng, or Schinsent (U. S. P. 1842 to 1882) is the root of *Panax quinquefolium* and *P. ginseng*, perennial herbs, the former growing in rich woods in the eastern United States and Canada, and the latter indigenous to the mountainous forests of eastern Asia and cultivated in northern China, Korea and Japan. The roots are gathered from three- to six-year-old plants, carefully cleaned and dried. The drug is extensively used in China and it has been estimated that about 300,000 pounds of ginseng are exported annually from the United States. The supplies are not only obtained from wild plants, but also from plants cultivated especially in Wisconsin, Michigan and Oregon.

The drug is cylindrical or fusiform, from 5 to 12 cm. in length, and 1 to 2.5 cm. in thickness; externally light yellowish brown, distinctly annulate in the upper portion and terminated at the crown by one or more stem-scars; lower portion very much wrinkled, occasionally branching and marked by a number of root-scars; fracture short; internally light yellowish brown, marked by a distinct dark brown cambium zone, a distinctly radiate wood and numerous oil-secretion canals, which in older roots have a brownish red resinous content; odor slightly aromatic; taste sweetish, mucilaginous and slightly bitter.

The active principle of ginseng appears to be a glucosidal substance, panaquilon. It also contains a saponin; a bitter principle; a volatile oil containing a camphoraceous substance; resin; sugar; mucilage; and starch.

USES AND DOSE.—Ginseng is a stimulant and a stomachic. It is a favorite remedy in Chinese medicine. Average dose, 2 gm.

Chinese Ginseng is yellowish brown and translucent, and has a bitter, followed by a sweet and mucilaginous taste. **Japanese Ginseng** is spindle-shaped, light yellow, hard and woody. **Korean Ginseng** is usually much branched, yellowish brown or light brown; the roots being still attached.

Panax Repens is the rhizome of *Panax repens*, a plant growing in Japan, and is considered to have properties similar to those of ginseng. The rhizome is horizontal, nearly cylindrical, more or less curved, from 5 to 10 cm. in length and 3 to 6 mm. in thickness, externally yellowish white, nodes considerably thickened and marked on the upper surface by circular stem-scars; the fracture is horny; internally it is whitish, marked by small yellowish oil-secretion canals in the cortex, narrow wedges of collateral fibrovascular bundles separated by broad medullary rays and a large pith.

Panax Repens contains 20 per cent of saponin which is also present in other members of the *Araliaceæ*, as *Panax fruticosum*, of tropical Asia; *Aralia montana* of Java; *Polyscias nodosa* of the Malay Peninsula; *Hepatpleurum venulosum* of tropical Asia and Australia; and *Trevesia sundaica* of Java.

UMBELLIFERÆ, OR CARROT FAMILY

This is a family of about 270 genera and 2700 species of herbs, which are widely distributed, being most abundant in the temperate zones. The leaves are alternate and mostly decompound; the flowers are always arranged in umbels (Fig. 248); the fruit is a cremocarp, the morphological characters of which are relied upon in the taxonomic study of the species. The plants resemble the *Araliaceæ* in that schizogenous secretory canals are found in the cortex, pericycle, pith, leaves and fruits, the contents of the canals being volatile oil, resin or gum. There is usually a collenchymatous thickening of the cell walls of the primary cortex, corresponding to the ribs of the stems and fruits. Medullary vascular bundles occur in several modifications in the stem. The vascular bundles in the petiole are always isolated. The pith of the internodes is usually hollow. Calcium oxalate is in the form of rosette aggregates, or as solitary crystals. Non-glandular hairs are occasionally present and may be unicellular, stellate, multiseriate or abietiform. Glandular hairs are wanting.

ANISE

Anise or Aniseed (U. S. P. 1820 to 1926; N. F. 1926 to date) is the dried ripe fruit of *Pimpinella Anisum* Linné. *Pimpinella* is Latin meaning two-winged, referring to the bipinnate leaves; *anisum* is the old Arabic name for anise.

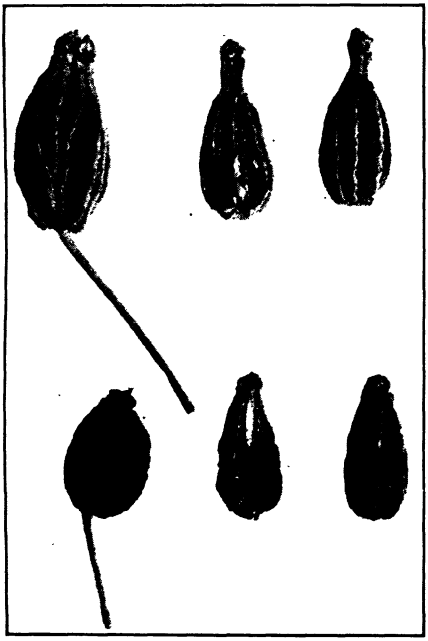


FIG. 246.—Italian anise, photo above, and Russian anise, photo below. Magnified six times. (Photo by Adamson.)

The plant is an annual herb indigenous to Asia Minor, Egypt and Greece, and cultivated in South America, Germany, Spain, Italy and southern Russia. The drug is derived from cultivated plants, and that obtained from Spain, known as "Alicante Anise," is preferred. Russian Anise is used chiefly for the distillation of the volatile oil.

Anise is among the oldest known medicines and spices. It was mentioned by Theophrastus, Dioscorides and Pliny and was one of the plants cultivated on the imperial farms of Charlemagne in the ninth century.

DESCRIPTION AND STRUCTURE.—See Figures 246, 247 and the National Formulary.

POWDER.—Color moderate yelowish brown to light olive brown; odor and taste agreeable, aromatic, and characteristic; non-glandular hairs, one-celled, up to 200 microns long, frequently curved, with numerous slight centrifugal projections; aleurone grains of the endosperm about 6 microns in diameter and enclosing a calcium oxalate rosette about 4 microns in diameter in each grain; fragments of pericarp with light brownish, branching, oil tubes.

CONSTITUENTS.—Volatile oil (1 to 3 per cent), consisting of about 80 to 90 per cent of anethole; fixed oil, 3 to 4 per cent; calcium oxalate. Total ash, about 7 per cent; acid-insoluble ash, 0.26 per cent.

USES AND DOSE.—Anise is an aromatic stimulant and carminative. It is also a diuretic and diaphoretic. It is largely used as a flavor. Anise fruits are used in certain types of bakery products of which the German Christmas cakes known as Springerle are an example. Average dose, 0.5 gm.

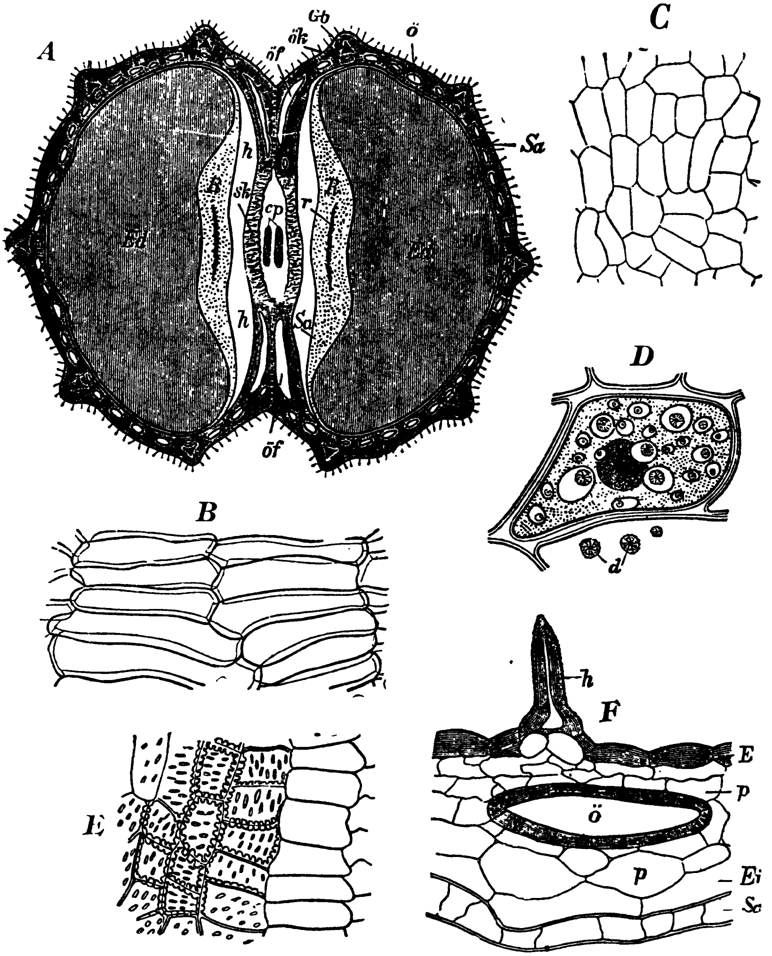


FIG. 247.—Anise: *A*, Transverse section of cremocarp showing carpophore (*cp*); wide vittæ (*öf*) on ventral (commissural) surface and smaller vittæ (*ö*, *ök*) between the ribs on the dorsal surface; fibrovascular bundles of ribs (*Gb*); sclerenchymatous fibers (*sk*); an air cavity in the wall of the pericarp on the ventral side (*h*); raphé tissue (*R*) with fibrovascular bundle (*r*); seed coat (*Sa*); and endosperm (*Ed*). *B*, Inner epidermis of pericarp. *C*, Epidermis of seed coat. *D*, Cell of endosperm showing a number of aleurone grains containing small rosettes of calcium oxalate, a large nucleus in the center of the cell, and a few isolated aggregates of calcium oxalate (*d*). *E*, Sclerenchymatous cells of the inner epidermis of the pericarp in the neighborhood of the carpophore. *F*, Transverse section of pericarp and seed coat showing epidermal cells (*E*) and a non-glandular hair having thick lamellated walls (*h*), parenchyma (*p*), a vitta (*ö*), inner epidermis (*Ei*) and seed coat (*Sa*). (After Meyer.)

ADULTERANTS.—Italian anise may be admixed with conium, which is distinguished by the absence of hairs and vittæ and the presence of coniine; the latter is determined by the development of the characteristic mouse-like odor on rubbing up the powder with alkalis or placing it in a solution of potassium or sodium hydroxide. The following microchemical tests may be useful in determining the presence of coniine, which occurs in the parenchyma and epidermal cells of the fruit; ammonium vanadate and sulfuric acid produce a blue color; iodine solution gives a reddish brown color; and picric acid gives a granular precipitate. Small lumps of clay and stones about the size of anise are frequently present.

Pimpinella or Pimpernel (N. F. 1916 to 1926), consists of the dried roots of *Pimpinella saxifraga* and *P. magna*. It occurs in fusiform pieces about 8 to 10 cm. in length, 4 to 10 mm. in diameter; externally yellowish brown; fracture short; internally whitish with numerous yellowish resin canals; the taste is acrid, pungent and aromatic. The drug contains a volatile oil; an acrid resin; a tasteless crystalline principle, pimpinellin; about 8 per cent of sugar; starch, and tannin. It is a diuretic and a diaphoretic.

Anise Oil (U. S. P. 1820 to date) is the volatile oil distilled with steam from the dried ripe fruit of *Pimpinella Anisum* Linné or from the dried ripe fruit of *Illicium verum* Hooker filius, Fam. *Magnoliaceæ* (Chinese Star Anise Oil, U. S. P. 1882 to 1894, 1905 to date).

Anise Oil is obtained largely from Spain, southern Russia, and Bulgaria, while Star Anise Oil is distilled in southern China. The oils are much alike in constituents and physical properties. Anise Oil is a colorless or pale yellow strongly refractive liquid having the characteristic odor and taste of anise. Consult the Pharmacopœia for its physical and chemical constants.

CONSTITUENTS.—Anethole, from 80 to 90 per cent or more; methylchavicol; oxidation products, such as anisic aldehyde and anisic acid, terpenes such as *d*-pinene and phellandrene, and probably some safrol in the oil from star anise.

If solid matter has separated, carefully warm the mixture at a low temperature until it is completely liquefied, and mix it thoroughly before using. Oil of anise is free from phenols and heavy metals.

USES AND DOSE.—Anise Oil is a carminative and flavoring, used as a corrigent with cathartic remedies to prevent griping, and is frequently combined with licorice. Average dose, 0.1 cc.

Anethole (N. F. 1916 to date) is parapropenyl anisole, $C_6H_4.C_3H_5OCH_3$. It is obtained from anise oil and other sources or is prepared synthetically. Anethole is a colorless or faintly yellow liquid at or above 23° C. At about 21° C. it solidifies to a crystalline mass which melts at 22° to 23° C. Anethole should be free from phenols, aldehydes and ketones. Consult the National Formulary for its physical and chemical constants.

USES AND DOSE.—Anethole is a carminative and flavor. Average dose, 0.1 cc.

FENNEL

Fennel or Fennelseed (U. S. P. 1820 to 1926; N. F. 1926 to date) is the dried ripe fruit of cultivated varieties of *Fœniculum vulgare* Miller. *Fœniculum* is Latin, meaning hay, in allusion to the odor of the plant.

The plants are perennial herbs (see Fig. 248) indigenous to the Mediterranean region of Europe and Asia, and cultivated in central and eastern Europe, Russia, India and Japan. The drug obtained from Saxony, Thuringia, Galicia and Russia is preferred.

DESCRIPTION AND STRUCTURE.—See Figures 249, 250, 253 and the National Formulary.

Powder.—Yellowish brown; aromatic; endosperm fragments, colorless and irregular, the cells filled with aleurone grains, each containing a rosette of calcium oxalate and a small globoid; fragments containing yellowish brown oil-tubes, the latter up to 200 microns in width; fibers and tracheæ few; mounts in chloral T.S. show numerous globules of fixed oil.

Constituents.—Volatile oil, 2 to 6.5 per cent; fixed oil, about 12 per cent. Total ash, 7.95 per cent; acid-insoluble ash, 0.45 per cent.

Uses and Dose.—Fennel is an aromatic stimulant, a carminative and a stomachic. It is used largely as a flavoring agent. Average dose, 1 gm.

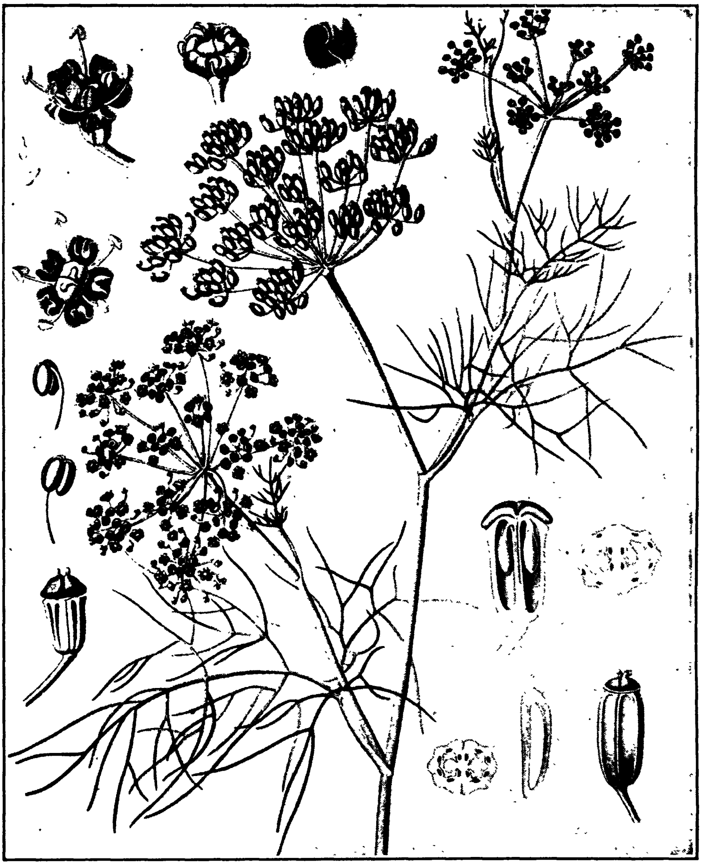


Fig. 248.—*Fœniculum vulgare,* showing the typical umbel. (After Köhler.)

Adulterations.—**Bitter Fennel,** the fruit of *Fœniculum piperitum,* has been substituted. The fruits are much smaller, decidedly bitter and the volatile oil is different in aroma. Fennel is frequently contaminated with wheat screenings, undeveloped fruits, various other umbelliferous fruits and dirt.

Allied Drugs.—The **Sweet or Roman Fennel,** obtained from plants (*F. dulce*) cultivated in southern France, yields about 2 per cent of oil containing considerable anethole but no fenchone. The more or less fusiform root of *Fœniculum vulgare* is also used like fennel. It is 8 to 15 cm. in length, of an aromatic odor and taste and contains a volatile oil, resin, starch and sugar.

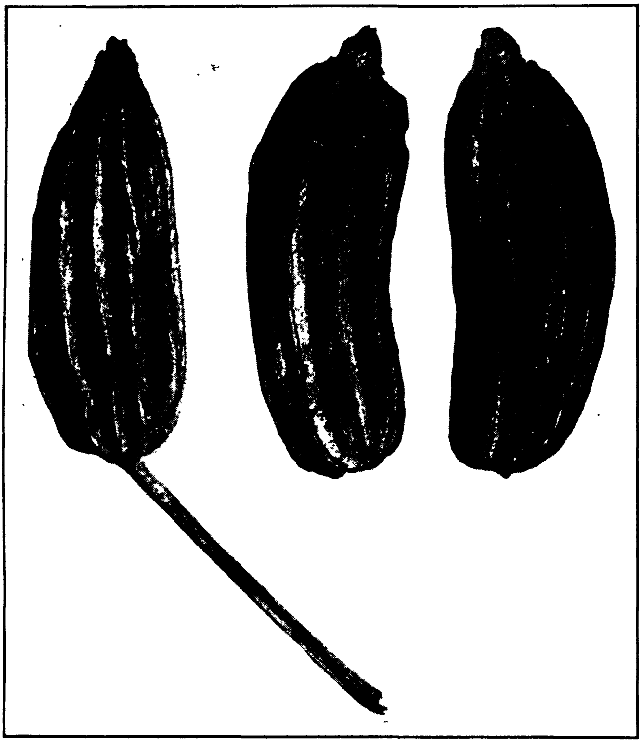


FIG. 249.—Fennel Fruit magnified 6 times. (Photo by Adamson.)

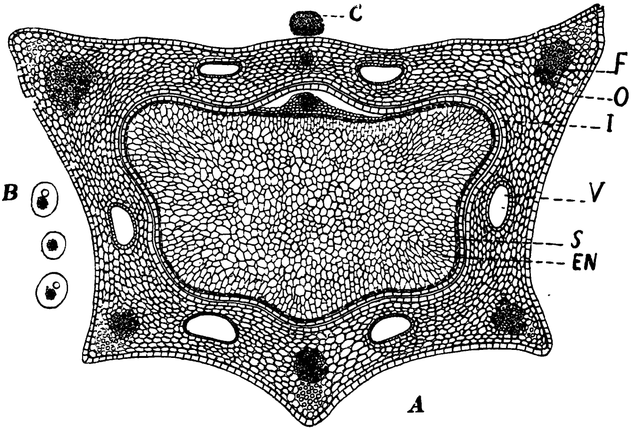


FIG. 250.—*A*, Transverse section through a mericarp of fennel: *O*, outer epidermis of pericarp; *I*, inner epidermis of pericarp; *F*, fibrovascular bundles; *V*, vittæ or oil canals; *S*, seed coat; *EN*, endosperm. *B*, Isolated aleurone grains from cells of endosperm of fennel showing globoids and small rosette aggregates of calcium oxalate. *C*, Section through the carpophore, which is composed chiefly of sclerenchymatous cells.

Fennel Oil (U. S. P. 1820 to date) is the volatile oil distilled with steam from the dried ripe fruit of *Fœniculum vulgare* Miller.

Oil of fennel is a colorless or pale yellow liquid, having the characteristic odor and taste of fennel. Consult the U. S. Pharmacopœia for its physical and chemical constants.

CONSTITUENTS.—Oil of fennel contains from 50 to 60 per cent of anethole; about 20 per cent of fenchone, which gives the fruit its characteristic odor and taste; chavicol, anisic aldehyde, anisic acid; *d*-pinene and dipentene. Macedonian fennel oil contains anethole, some limonene and phellandrene, but no fenchone; wild bitter fennel oil contains scarcely any anethole, but consists in part of phellandrene and fenchone.

If solid material has separated, the oil should be carefully warmed at a low temperature until it is completely liquefied and then thoroughly mixed. Oil of fennel is free from heavy metals.

USES AND DOSE.—Oil of fennel is a carminative, an aromatic and a flavor. Average dose, 0.1 cc.

CARAWAY

Caraway, or Carawayseed (U. S. P. 1820 to date) is the dried ripe fruit of *Carum Carvi* Linné. The generic name *Carum* is probably from the Latin *careum*, derived from Caria, a country of Asia Minor; *carvi* is Latin for *carvy*, the Scotch name for caraway. Medieval pharmacists called the drug *Carui*. The plant is a biennial herb indigenous to Europe and Asia and cultivated in England, northern Europe, Morocco and the United States, being naturalized in northern United States and parts of Canada. The drug is gathered when the fruits are ripe, that grown in Holland being preferred.

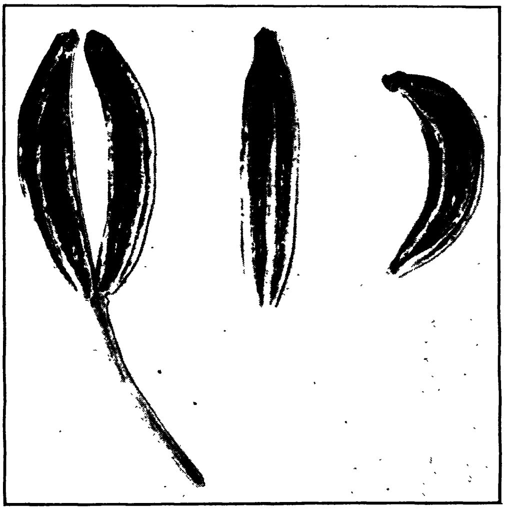


FIG. 251.—Caraway Fruits. Magnified 6 times. (Photo by Adamson.)

Caraway fruits were known to the Arabians who called them *Karawya.*

DESCRIPTION, STRUCTURE AND POWDER.—See Figures 251, 253 and the U. S. Pharmacopœia.

CONSTITUENTS.—Volatile oil, from 5 to 7 per cent; fixed oil; proteins; calcium oxalate. Total ash, 6.4 per cent, with about 0.5 per cent of acid-insoluble ash.

USES AND DOSE.—Caraway is an aromatic, a stimulant, a carminative; also a diuretic and a diaphoretic. Caraway fruits are used as a flavoring spice in bread, cakes and other articles of food. Average dose, 1 gm.

ALLIED DRUGS.—The seeds of *Nigella sativa* and *N. damascena* (Fam. *Ranunculaceæ*) are used in medicine and for flavoring like caraway. They are commonly known as **Black Caraway.** The seeds are ovoid, 3- to 4-angled, about 3 mm. in length; externally black and reticulate; internally, having a large, oily reserve layer in which is embedded the small, greenish embryo. Black caraway contains 1.5 per cent of a volatile oil; 1.5 per cent of a glucoside, melanthin, which resembles saponin and helleborin; a fluorescent alkaloid, damascenin, giving the volatile oil from *N. damascena* its fluorescence; another alkaloid, connigelline; and about 35 per cent of a fixed oil.

Indian Dill-seed (*Peucedanum sowa*) has been sold as a substitute for caraway but it is very inferior to the Dutch caraway. **Mogador Caraway** from Morocco is suitable only for distilling oil for perfuming soap. **Levant Caraway** from Tunis, a novelty in the London market, is the most acceptable substitute for the Dutch article so far offered. **North Russian Caraway** is especially suited for the flavoring of the liqueur known as **kümmel,** but yields very little volatile oil.

Caraway Oil (U. S. P. 1831 to 1936; N. F. 1936 to date) is a volatile oil distilled from the dried ripe fruit of *Carum Carvi* Linné, and yields not less than 50 per cent by volume, of carvone.

Oil of caraway is a colorless or pale yellow liquid, with the characteristic odor and taste of caraway. Consult the National Formulary for its physical and chemical constants.

CONSTITUENTS.—Oil of caraway contains 50 to 60 per cent of the ketone carvone and from 40 to 50 per cent of the terpene *d*-limonene with small amounts of carveol and dihydrocarvone. (Carvone is a derivative of limonene and the simultaneous occurrence of these compounds in oil of caraway is particularly interesting.)

USES AND DOSE.—Oil of caraway is a carminative, a stimulant and an aromatic. Average dose, 0.1 cc.

CORIANDER

Coriander or Corianderseed (U. S. P. 1820 to 1926; N. F. 1926 to date) is the dried ripe fruit of *Coriandrum sativum* Linné, and yields not less than 0.25 cc. of volatile coriander oil from each 100 gm. of drug. *Coriandrum* is from the Greek *Koris,* a bedbug, and refers to the disagreeable odor of the young plant; *sativus* means sown or cultivated. The plant is an annual herb indigenous to the Mediterranean and Caucasian region, naturalized in the temperate parts of Europe and cultivated there and in Africa and India. The fruit is threshed when full grown from cultivated plants and then dried. The drug from Russia and Thuringia is preferred.

Coriander was mentioned by the early Sanskrit writers and in the Mosaic books, Exodus and Numbers, and occurs in the papyrus of Ebers (1550 B.C.). Cato as well as Pliny also mention it and Charlemagne included it in the list of valuable products.

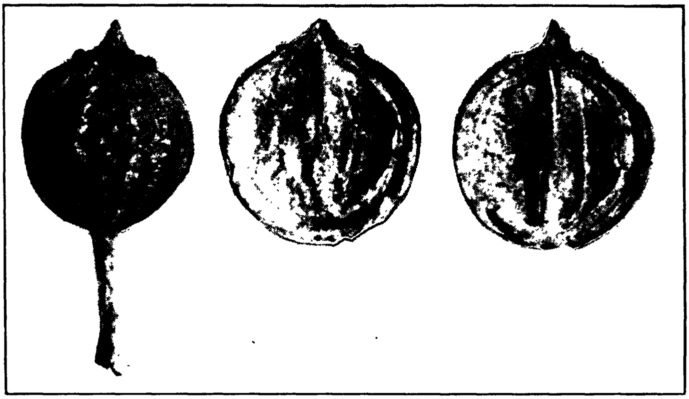


Fig. 252.—Coriander Fruit. Magnified 6 times. (Photo by Adamson.)

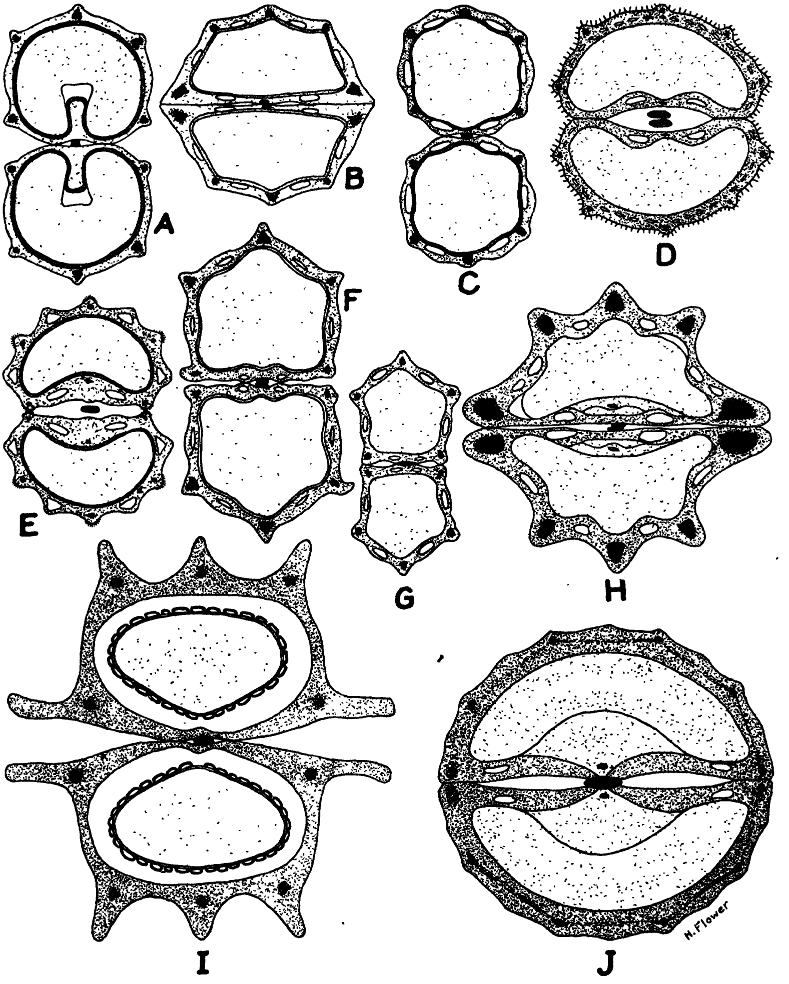


Fig. 253.—Some Umbelliferous Fruits in transverse section, as seen in lens view and al drawn to the same scale: *A*, Conium; *B*, Dill; *C*, Parsley; *D*, Anise; *E*, Cumin; *F*, Caraway *G*, Celery; *H*, Fennel; *I*, Angelica; *J*, Coriander. (Drawings by Harry Flower.)

Description, Structure and Powder.—See Figures 252 and 253 and the National Formulary.

Constituents.—Volatile oil, 0.5 to 1 per cent; fixed oil, about 13 per cent; tannin; calcium oxalate. Total ash, about 5.3 per cent, acid-insoluble ash, 0.3 per cent.

Uses and Dose.—Coriander is an aromatic stimulant and a carminative. Average dose, 0.5 gm.

Allied Product.—**Bombay or Indian Coriander** is the fruit of a variety of *Coriandrum sativum* imported from Bombay. The fruits are oval and yield less volatile oil than the official drug.

Coriander Oil (U. S. P. 1882 to date) is the volatile oil distilled with steam from the dried ripe fruit of *Coriandrum sativum* Linné. Oil of coriander is a colorless or pale yellow liquid, having the characteristic odor and taste of coriander. Consult the U. S. Pharmacopœia for its physical and chemical constants.

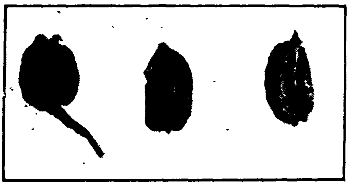
Constituents.—Oil of coriander contains from 50 to 80 per cent of *d*-linalool (coriandrol); the hydrocarbons pinene and terpinene and small quantities of borneol and geraniol.

Uses and Dose.—Oil of coriander is a carminative and an aromatic. Average dose, 0.1 cc.

CELERY FRUIT

Celery Fruit or Celeryseed (N. F. 1916 to 1947) is the dried ripe fruit of *Apium graveolens* Linné. *Apium* is the Latin for parsley and refers to the resemblance between the two plants; *graveolens* is Latin meaning to emit a heavy odor. The plant is a biennial herb, indigenous to England and extensively cultivated throughout the temperate regions of Europe and the United States, for its succulent leaf-stalks or fleshy roots and in France for its aromatic fruits, all of these being used for culinary purposes.

The fruits are also used to a limited extent in medicine.



Celery Fruits.Fig. 254.—Magnified 6 times. (Photo by Adamson.)

Description, Structure and Powder.—See Figures 253, 254 and the National Formulary, Seventh Edition.

Constituents.—A colorless volatile oil, from 2.5 to 3 per cent, consisting of *d*-limonene and 90 per cent of hydrocarbons. The fresh celery leaves yield about 0.1 per cent of a volatile oil, having a greenish yellow color and forming a clear solution with 10 parts of 90 per cent alcohol.

Standards.—Celery fruit contains not more than 5 per cent of foreign organic matter, and yields not more than 3 per cent of acid-insoluble ash, and not less than 1.75 cc. of volatile oil of celery fruit from each 100 gm. of drug.

Uses and Dose.—Celery fruit is an aromatic stimulant, a carminative and a stomachic. Average dose, 1 gm.

Unofficial Umbelliferous Fruits

Conium or Poison Hemlock (U. S. P. 1831 to 1863, 1873 to 1916; N. F. 1916 to 1936) is the dried, full-grown but unripe fruit of *Conium maculatum*, a large biennial herb indigenous to Europe and naturalized in North and South America and in various parts of Asia. The fruit is collected, when full grown but still green, from wild plants, and carefully dried and preserved. The juice of this plant entered into the famous hemlock potion of the Greeks and was employed by them in putting their criminals to death. Tradition has it that Socrates was put to death with a decoction of this plant.

The mericarps are usually separate; the cremocarp is broadly ovoid, slightly compressed laterally, 3 to 4 mm. in length, about 2 mm. in diameter with a pedicel 3 to 5 mm. in length; externally, it is a grayish green with 10 straight more or less crenate yellowish ribs and depressed stylopodium; a slender carpophore is attached to each mericarp; internally greenish brown, 5-angled or somewhat reniform in cross-section and without vittæ; seed reniform, with a deep furrow on the commissural side, and with a small embryo at the upper end of the reserve layer; odor slight; when crushed in a solution of a fixed alkali, a strong, disagreeable, mouse-like odor develops; taste disagreeable, somewhat acrid.

For the structure see Figures 253 and 256.

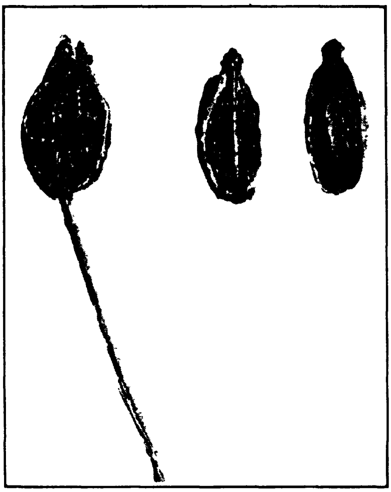


Fig. 255

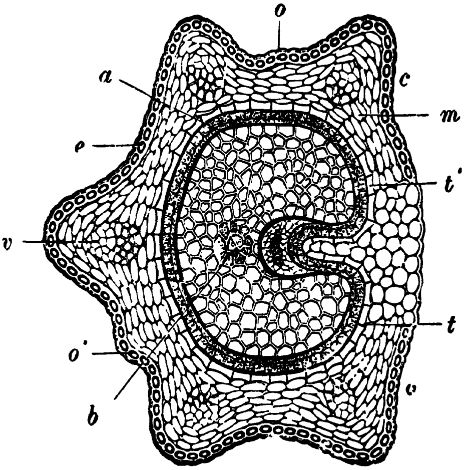


Fig. 256

Fig. 255.—Conium Fruit. Magnified 6 times. (Photo by Adamson.)

Fig. 256.—Cross-section of a mericarp of conium: *c*, *c*, commissural surface; *e*, portion without secondary ribs; *o*, portion showing slight development of secondary rib; *o'*, secondary rib; *v*, fibrovascular bundle of pericarp (*m*); *t*, *t'*, layer containing coniine; *a*, endosperm; *b*, tissue of the embryo. (After Flückiger.)

The constituents are: the liquid alkaloid coniine (hexahydropropyl pyridine), 0.5 to 3 per cent; conhydrine (hydroxyconiine), in plates, dextrorotatory, and very poisonous; pseudoconhydrine (an isomer of conhydrine), in needles; γ-coniceine, a colorless, oily alkaloid with a disagreeable odor and 18 times more poisonous even than coniine; fixed oil; starch; calcium oxalate; about 6 per cent of total ash and 0.35 per cent of acid-insoluble ash.

Coniine is naturally combined in the drug with organic acids; it may be readily extracted with ether after alkalinization of the drug. Pure coniine is a colorless, nearly odorless liquid and forms a number of crystalline salts. Coniine becomes blood-red and afterwards green, with concentrated sulfuric acid. Phosphotungstic acid and Marme's reagent are the most satisfactory reagents for the microcrystalline identification of coniine. The disagreeable odor in commercial coniine, as well as in conium, is due to the alkaloid coniceine.

Conium is an antispasmodic, a sedative and an anodyne. It acts on the peripheral ganglia in a manner similar to nicotine. Conium was formerly used to a considerable extent in medicine, but today has fallen into almost complete disuse. It is of considerable interest, however, that coniine was one of the first alkaloids discovered (1827) and the first to be prepared synthetically (Ladenburg, 1886).

The entire fresh plant of *Conium maculatum* is used in the preparation of **Succus Conii** (U. S. P. 1873 to 1882). It probably contains the same constituents as the fruit, but in smaller amounts. The root contains 0.018 to 0.047 per cent of total alkaloids; the stems 0.064 per cent; the leaves 0.187 per cent and the flowers and flower stalks 0.236 per cent. Dried conium leaves and flowering tops, **Conii Folia** (U. S. P. 1820 to 1882) have been used in medicine for the same purposes as conium fruit.

Æthusa, the poisonous leaves of the Lesser Hemlock or Fool's Parsley (*Æthusa cynapium*) have been substituted for conium leaves. The leaflets are rhomboid-oval, deeply lobed, the segments being sometimes further lobed, narrow to linear, abruptly pointed or blunt. The fruit has broad cork-like ribs.

Water Hemlock (*Cicuta maculata*) is a stout perennial herb growing in wet meadows throughout the United States and Canada. The stems are streaked with purple, the leaves are pinnately compound, the leaflets being oblong-lanceolate and coarsely serrate; the flowers are white, occurring in large compound umbels. The fruit is ovoid, with prominent ribs and six conspicuous vittæ. The rhizome is large and fleshy and is sometimes mistaken for parsnip; it contains a resinous substance, cicutoxin, which is quite poisonous. The fruits contain a volatile alkaloid, cicutine, resembling coniine, and a volatile oil resembling oil of cumin.

Petroselinum or Parsley Root (U. S. P. 1820 to 1872; N. F. 1916 to 1926) and **Petroselinum, Parsley Fruit or Parsleyseed** (U. S. P. 1916 to 1926) are the dried root and the dried ripe fruit, respectively, of *Petroselinum sativum* Hoffman. The plant is a biennial herb indigenous to southern Europe and Asia Minor and extensively cultivated, the leaves being used as a seasoning herb for culinary purposes. Pliny states that in his time there was not a salad or sauce used upon the table that did not contain it. The fruits are gathered in the fall and carefully dried.

The root drug occurs in irregular slices, light yellowish in color, with short fracture, and containing numerous oil-secretion canals. Odor is aromatic, taste sweetish and slightly pungent. The fleshy root may be cooked and eaten like parsnips.

The fruits are small, up to 3 mm. long, with the usual appearance and structure of Umbelliferous fruits; see Figures 257 and 253. The fruit contains 1 to 3 per cent of volatile oil consisting of a stearoptene, apiol, and a terpene, probably *l*-pinene; a fixed oil, 6 per cent; resinous substances, 5 per cent; mucilage, 7 per cent; fat, resembling stearic acid, 16.5 per cent; phyteumacolla, combined with potassium salts, 12.5 per cent; protein substances, combined with calcium phosphate, 3 per cent; crude fiber, 48.5 per cent; ash, 4 to 6 per cent.

Parsley fruits and herb are extracted with ether to prepare the oleoresin known as **Liquid Apiol** (U. S. P. 1916 to 1926). It is a dark green, thick, oily, non-volatile liquid with an aromatic odor. If only the ripe fruit is used, the extract is yellow to brown in color. In doses of 0.2 gm. it is a diuretic and stimulant; in doses of 0.5 gm. it is an antiperiodic and an emmenagogue

Apiol occurs as white, optically inactive crystals; heavier than water, insoluble in water, but soluble in other usual solvents. Sometimes it is obtained from the fruit of the East Indian Dill, *Peucedanum sowa*, which is apparently isomeric with the apiol from parsley oil.

Heracleum, Masterwort or Cow-parsnip (U. S. P. 1820 to 1863) is the root of *Heracleum lanatum* Linné. The plant is a wooly perennial herb growing up to 3 meters high in northern and central United States to the Pacific Ocean. All parts of the plant have a rank odor and a pungently acrid taste. The root, leaves and fruit have been employed medicinally. A volatile oil, a resin and acrid principles are present in the plant. It has been employed as a vesicant (fresh leaves), a counter-irritant and as a gastro-intestinal irritant. Dose, up to 4 gm.

Carrot Fruit or Wild Carrotseed (U. S. P. 1820 to 1882) is the ripe fruit of *Daucus Carota* Linné. The fruit is small, about 3 mm. long, and has a slightly aromatic odor and a pungent taste. The root of the wild plant is thin, spindly, woody, white, of an aromatic odor and a pungent, bitter taste. The fruit is used as a diuretic, stimulant and a menstrual excitant.

Eryngo or Button Snakeroot (U. S. P. 1820 to 1873) is the rhizome of *Eryngium yuccæfolium*, a plant with long, grass-like, fringed, radical leaves, a tall flower stalk, with short leaves and a dense head of white flowers. It is found in pine barrens and prairies from New Jersey to Wisconsin and southward.

The rhizome consists of a short root stalk and numerous branches with a heavy aromatic odor and an aromatic, sweetish, somewhat acrid taste. It was used as a diaphoretic, expectorant and emetic.

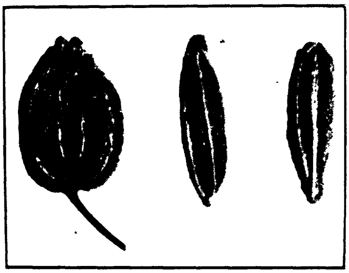


Fig. 257.—Parsley Fruit. Magnified 6 times. (Photo by Adamson.)

Anethi Fructus or Dill Fruit consists of the dried ripe fruit of *Anethum graveolens.* The plant is a small annual herb indigenous to southern Europe and cultivated in England, Germany, Roumania, and the United States. It is used extensively as a pickling spice, and like other umbelliferous fruits has carminative and stimulant properties. The oil is usually distilled from the fresh or partially dried, whole herb when in fruit, much as peppermint oil is prepared.

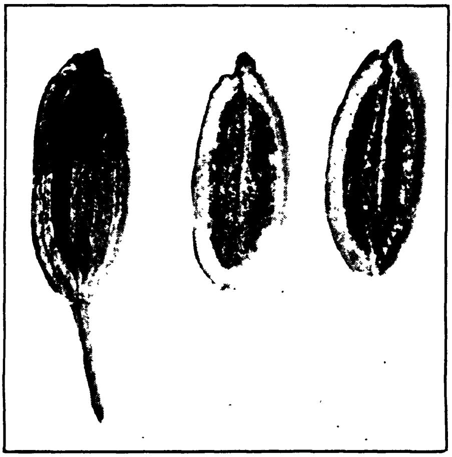


Fig. 258.—Dill Fruit. Magnified 6 times. (Photo by Adamson.)

Angelica or Angelica Herb (U. S. P. 1820 to 1863); **Angelica or Angelica Root** (U. S. P. 1863 to 1873;N. F. 1916 to 1936); **Angelicæ Fructus, Angelica Fruit or Angelicaseed** (U. S. P. 1831 to 1842; N. F. 1916 to 1936) are the dried leaves and flowering tops; the rhizome and roots; and the ripe fruit, respectively, of *Angelica archangelica* Linné and of other species of *Angelica.*

The plant is a biennial, up to 2 meters tall, indigenous to northern Europe and Siberia, extensively cultivated in Hungary, Germany, and to some extent in the United States. The fresh stalks are "candied" and used as an aromatic flavoring in cookery.

Angelica Oil, from the herb, about 0.1 per cent; from the root, 0.35 to 1 per cent; and from the fruit, about 1 per cent, is nearly colorless when fresh, but becomes brownish on keeping, and the odor resembles a mixture of pepper and musk.

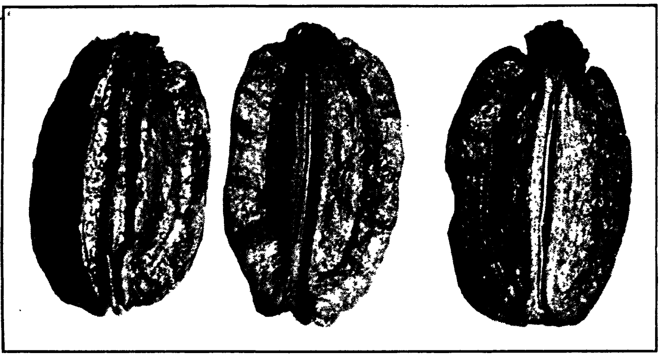


Fig. 259.—Angelica Fruit. Magnified 6 times. (Photo by Adamson.)

The large, fleshy roots are gathered in the fall, sliced, carefully dried, and preserved against insects. The fruits are large, up to 8 mm. in length, with 6 strong ribs or wings, and about 20 large oil canals (see Figs. 253 and 259).

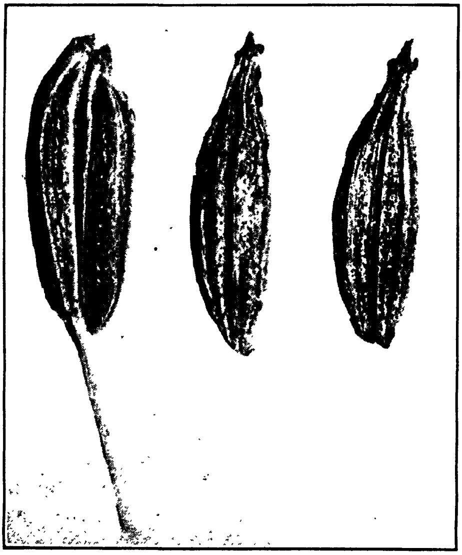


Fig. 260.—Cumin Fruit. Magnified 6 times. (Photo by Adamson.)

Angelica is an aromatic, a stimulant, a carminative and a stomachic. Average dose of root or fruit, 1 gm.

Cumin consists of the dried ripe fruit of *Cuminum cyminum*, a small annual herb indigenous to Egypt. It is widely cultivated and most commercial supplies come from Sicily, Malta and India. Cumin fruits are about 6 mm. long and somewhat resemble caraway. They are covered with short bristly hairs. The fruits contain from 2 to 4 per cent of a volatile oil which consists of from 25 to 35 per cent of cuminic aldehyde. It was a common spice in the Middle Ages but is now principally employed in veterinary practice.

Sumbul or Musk Root (U. S. P. 1882 to 1926; N. F. 1926 to 1947) consists of the dried rhizome and roots of *Ferula sumbul* (Kaufmann) Hooker filius, or of other closely related species of *Ferula* possessing a characteristic musk-like odor. *Ferula* is the Latin name for the fennel plant, from the Latin *ferio*, to strike; *sumbul* is from the Arabic, signifying an ear or spike. The plant is a perennial herb indigenous to Turkestan. The root has long been used in India and Persia as a perfume and incense in religious ceremonies. Russian physicians were the first to employ it in Europe and it still enters the European markets by way of Leningrad.

The drug occurs in transverse segments, up to 7 cm. in diameter, and floats in water; externally brown, distinctly annulate, periderm easily separable; the upper part of the rhizome with occasional circular scars, stem bases and leaf remnants consisting of stout fibers; fracture short, irregular, but fibrous; internally light yellow, resinous, spongy, porous, the wood wedges irregular, due to anomalous secondary cambiums.

The cork is thin with yellowish brown cell walls; cortex of irregularly twisted strands of sieve and parenchyma; easily separable, radiate wood wedges and medullary rays; pith small. The oleoresin secretion canals are large, uniseriate, numerous, with reddish brown or brownish black contents.

The powder is grayish brown to dark brown; odor musk-like; taste bitter and pungent; tracheæ usually with scalariform perforations; large, irregular, brownish black fragments of oleoresin canals or reddish brown fragments of oleoresin; occasional fragments of yellowish brown cork; long, narrow fragments consisting of more or less collapsed sieve tissue; occasional fragments of well-defined parenchyma with a few small, nearly spheroidal starch grains.

The drug contains 0.3 to 1 per cent of volatile oil having the taste of peppermint; two balsamic resins; umbelliferon; a bitter principle; fixed oil, 17 per cent; and several acids, as angelic, valerianic and methyl crotonic. Total ash, 5.18 per cent with about 0.85 per cent of acid-insoluble ash.

Sumbul is a carminative, an antispasmodic and a nervine. Average dose, 2 gm.

ASAFETIDA

Asafetida or Gum Asafetida (U. S. P. 1820 to 1942; N. F. 1942 to date) is the oleo-gum-resin obtained by incising the living rhizomes and roots of *Ferula Assa-fœtida* Linné and *Ferula fœtida* (Bunge) Regel and of other species of *Ferula*. The Latin, *Asa*, means gum, or the Arabic *aza*, means healing, and the Latin *fœtida* refers to the ill-smelling, offensive odor of the drug.

The plants are perennial branching herbs, up to 3 meters high, indigenous to eastern Persia and western Afghanistan. The drug is collected as follows: (1) Remove the soil from the upper part of the large root; (2) transversely cut off the root crown; (3) protect the cut surface from the sun; (4) scrape off and save the milky exudation; (5) repeat the process every week or so during the summer or until the root is exhausted. Most of the drug is collected in eastern Persia and Afghanistan. Under the name of *Laser*, a substance supposed to be asafetida has been used in Persia and India since time immemorial. It appears in

Sanskrit works under the name of *Hingu*. It has long been employed by the Arabs, who no doubt introduced it into Europe during the Middle Ages.

Description.—A soft mass, sometimes almost semi-liquid, or in irregular masses of agglutinated tears, or in separate ovoid tears, from 1 to 4 cm. in diameter, which when fresh are tough, yellowish white and translucent, changing gradually to pinkish, violet-streaked, and finally reddish brown, and becoming, on drying, hard and brittle; internally the tears are milky white and opaque; odor persistently alliaceous; taste bitter, alliaceous and acrid.

To powder asafetida, which always impairs its quality, it is first dried at a temperature not higher than 30° C. or placed over freshly burned lime. It is comminuted, preferably at a low temperature, and diluents of starch or magnesium carbonate are sometimes added, in order to preserve it in the powdered form. It should be kept in tightly closed bottles.

Constituents.—Resin 45 to 60 per cent; volatile oil 3 to 17 per cent; gum up to 25 per cent. The reddish brown amorphous resin (consisting of the ferulaic ester of asa-resinotannol) yields on dry distillation, umbelliferon; on treatment with sulfuric acid, resorcin; and on fusion with potassium hydrate, protocatechuic acid. The volatile oil consists of hexenyl sulfide, hexenyl disulfide, pinene and cadinine. Also present are small amounts of ferulic acid (chemically related to vanillin, eugenol and cinnamic acid); vanillin, free asa-resinotannol, and formic, acetic, valeric and malic acids. Clean tears of asafetida yield 1 or 2 per cent of total ash, almost entirely soluble in diluted hydrochloric acid; dirty agglutinated drug may yield up to 50 per cent of total ash; carefully prepared drug yields less than 10 per cent of total ash.

Standards and Tests.—Asafetida yields not less than 50 per cent of alcohol-soluble extractive and not more than 15 per cent of acid-insoluble ash. Asafetida yields a milk-white emulsion when triturated with water, which becomes yellowish on the addition of alkali solution. For tests of identity and purity, see the National Formulary.

Uses and Dose.—Asafetida is a stimulant, an expectorant, an antispasmodic and a laxative. Average dose, 0.4 gm.

Adulterants.—Asafetida may contain other gum-resins, as galbanum or ammoniac, colophony, fragments of vegetable tissues, red clay, sand and stones; it is sometimes adulterated with dirty white, gritty masses of gypsum, at other times with barley or wheat flour or translucent gums.

Ammoniac (U. S. P. 1820 to 1905) is the gum-resinous exudation from *Dorema ammoniacum*, a perennial herb indigenous to central and eastern Persia and the deserts near the Arabian Sea. The gum-resin occurs in secretion canals throughout the plant, exudes as a result of insect punctures and hardens upon the stems and petioles. Most of the drug is sent to Bombay, where it is garbled. It occurs in irregular, somewhat rounded tears, from 5 to 20 mm. in diameter, occasionally agglutinated into larger masses; externally pale yellowish brown, brittle when cold and breaking with a flat, conchoidal and waxy fracture; internally yellowish white or light yellowish brown; odor distinct; taste bitter and acrid.

When triturated with water it yields a yellowish white emulsion, becoming reddish violet upon the addition of a few drops of a solution of chlorinated soda: or yellowish, becoming brown upon the addition of sodium hydroxide T.S. If 1 part of finely powdered ammoniac is boiled with 15 parts of hydrochloric acid, the solution filtered, and an excess of ammonia water added, the solution should show no blue fluorescence (absence of *galbanum*).

Ammoniac contains a volatile oil, from 0.2 to 0.4 per cent; an acid resin (which is an ester of ammoresinotannol and salicylic acid); an indifferent resin, from 60 to 70 per cent; a gum resembling acacia, from 12 to 16 per cent; a trace of free salicylic acid, several volatile acids, acetic and caproic; ash from 2 to 10 per cent. None of the constituents contains either sulfur or umbelliferon.

Ammoniac is a stimulant, a carminative, an antiseptic and an expectorant.

Galbanum is a gum-resinous exudation from *Ferula galbaniflua* and probably other species of *Ferula*, perennial herbs indigenous to the prairies of northern and western Persia and Afghanistan. The gum-resin occurs in schizogenous secretion canals throughout the plant and exudes as a result of natural wounds, the exudation being sometimes facilitated by incising the stems above the roots.

It occurs in irregular masses, occasionally in tears, usually admixed with fragments of vegetable tissues; from 0.5 to 7 cm. in diameter; externally bluish green or orange brown to almost brownish black, somewhat oily on the surface; becoming soft and sticky from the heat of the hand; when cold, dry and brittle; fracture somewhat granular and waxy; internally light yellow and shiny; odor balsamic; taste bitter and acrid.

Galbanum is only partly soluble in water or alcohol. When triturated with water, it yields a turbid milky fluid, which upon the addition of a drop of ammonia water assumes a bluish fluorescence. When galbanum is boiled with hydrochloric acid and the solution allowed to stand for an hour, it becomes bright red, changing to dark violet upon the addition of an equal amount of alcohol and heating to 60° C.

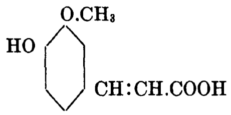
In order to powder galbanum the same means are employed as described under asafetida. It contains a volatile oil, 9.5 per cent; a resin soluble in alcohol, up to 63.5 per cent, which consists of 20 per cent of combined umbelliferon, 50 per cent of galbaresinotannol and 0.25 per cent of free umbelliferon. Gum and impurities up to 27 per cent; and ash 16 to 20 per cent.

Galbanum is a stimulant, a carminative, an expectorant and an antispasmodic.

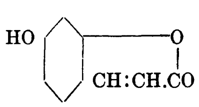
MICROCHEMISTRY OF ASAFETIDA, AMMONIAC AND GALBANUM

Asafetida, ammoniac and galbanum are usually designated as gum-resins; they are, however, oleo-gum-resins since they contain variable quantities of volatile oil. Each contains about 20 per cent of gum, the remainder consisting largely of resins composed of resinotannols combined with salicylic acid, umbelliferon or ferulic acid.

As coumarin is the lactone of coumarinic acid (hydroxy-cinnamic acid), thus umbelliferon is the lactone of umbellic acid (dihydroxy-cinnamic acid). Ferulic acid is methoxy-hydroxy-cinnamic acid. The structure of umbelliferon and ferulic acid is illustrated in the following formulas:



Ferulic acid



Umbelliferon

Salicylic Acid may be demonstrated in ammoniac by microsublimation. Add a drop of hydrochloric acid to a few milligrams of ammoniac, cover with a microsublimation ring and sublime. Too much heat must not be used or the salicylic acid will decompose into phenol and carbon dioxide. Salicylic acid sublimes in needles. The sublimate may be further identified by taking up in dilute sodium hydroxide and recrystallizing as sodium salicylate. Silver nitrate will give prisms of silver salicylate with sodium salicylate. The sublimate of salicylic acid is colored violet upon the addition of a drop of ferric chloride solution.

Umbelliferon occurs in the free state in galbanum, and in the combined state in galbanum and asafetida. It may be tested for by the fact that it gives a blue fluorescence with ammonia when in the free state. It is best extracted with alcohol, filtered and ammonia added. If in the combined state, the substance must first be boiled with hydrochloric acid, then diluted, filtered and ammonia added. Umbelliferon may be obtained by microsublimation, the sublimate occurring in clumps which later resolve into long needles.

CORNACEÆ, OR DOGWOOD FAMILY

This is a small family of shrubs and trees, comprising 16 genera and 85 species. The leaves are simple and opposite, and the flowers are arranged in cymes or heads, which in the case of the flowering dogwood (*Cornus florida*) are subtended by 4 large, petal-like, white or pinkish bracts. The pericycle contains isolated groups of bast fibers, or is made up of a composite and continuous ring of sclerenchyma. Secretory elements are seldom present. Calcium oxalate occurs as rosette aggregates, solitary crystals or microcrystals. The non-glandular hairs are mostly unicellular and are sometimes provided with verrucose thickenings of the cuticle. Glandular hairs of a number of special forms are present.

Cornus Circinata or Round-leaved Dogwood (U. S. P. 1820 to 1882); **Cornus, Cornus Florida, or Common Dogwood** (U. S. P. 1820 to 1894; N. F. 1916 to 1936); **Cornus Sericea or Swamp Dogwood** (U. S. P. 1820 to 1882) are, respectively, the dried bark of *Cornus circinata;* the dried root bark of *Cornus florida* Linné; and the dried bark of *Cornus sericea.*

Cornus florida is a small tree, rarely 12 meters high, and the other two plants are shrubs, all indigenous to the eastern United States from Canada to Virginia and Tennessee.

These three bark drugs, both from the stem and the root, are bitter and astringent, though the root barks usually contain more of the bitter principle, cornin, than do the stem barks. Cornus Sericea is more astringent than Cornus Circinata, more bitter than Cornus Florida. The "eclectic" cornin is a hydro-alcoholic dry extract prepared from Cornus Florida; it is strongly bitter and astringent.

The Cornus barks have been used as bitter tonics; during the Civil War, Cornus Florida was used in place of cinchona as an anti-malarial. Average dose, 2 gm. For a complete description of Cornus Florida see the National Formulary, Fifth Edition.

ERICACEÆ, OR HEATH FAMILY

This is a large family of nearly 1500 species of very wide geographic distribution; the species are mostly shrubs, erect or prostrate, occasionally small trees, and rarely herbs. The plants vary in their morphological characters; both glandular and non-glandular hairs commonly occur in a variety of forms.

The family can be divided on morphological grounds into 3 subfamilies: (1) the *Ericoideæ* proper, in the flowers of which the calyx is free from the ovary, and the stomata are surrounded by more than 2 epidermal cells. This subfamily includes *Rhododendron, Kalmia, Epigæa, Gaultheria* and other heath-like plants. (2) The *Vaccinioideæ,* or Whortle-Berry subfamily, in the flowers of which the calyx adheres to the ovary, the latter developing into an edible berry-like fruit, surmounted by the short calyx teeth. The stomata have 2 neighbor cells which lie parallel to the pore. This subfamily includes the blueberry and huckleberry plants. (3) The *Monotropoideæ,* or Indian Pipe subfamily are saprophytes and include the Indian Pipe and Beech Drops. Those *Ericaceæ* in which the flowers have a polypetalous corolla are sometimes placed in a separate subfamily, the *Pyroloideæ*, which comprises about 20 species, *Pyrola*, *Chimaphila* and possibly 2 other genera.

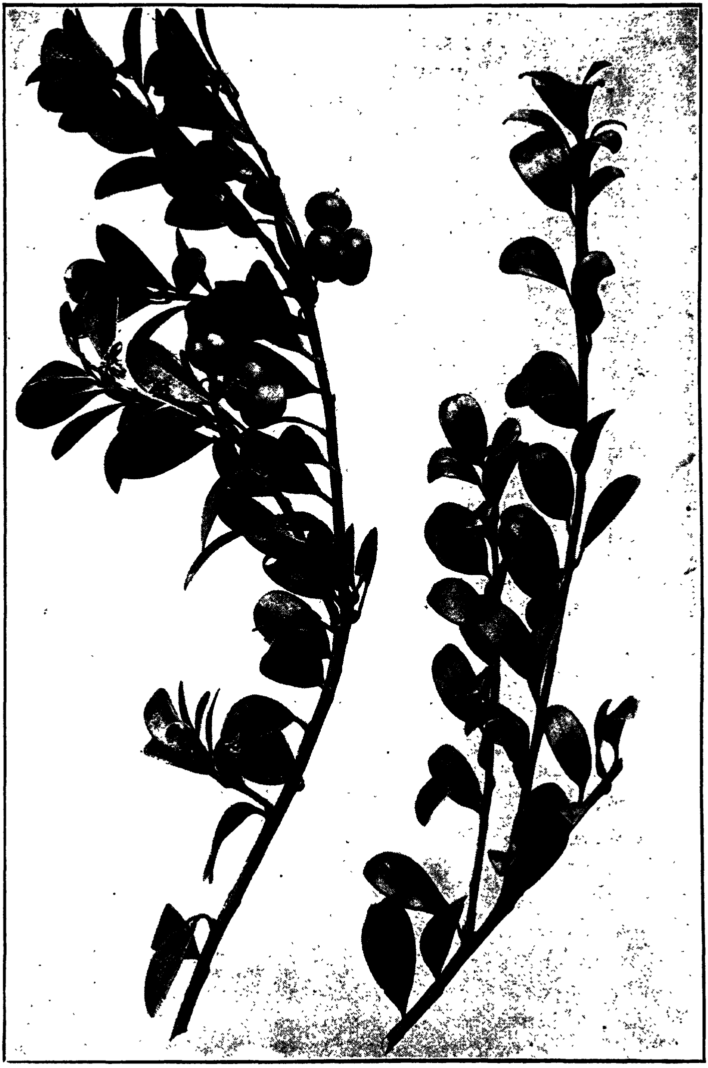


FIG. 261.—Bearberry (*Arctostaphylos uva-ursi*), a trailing, shrubby plant with thick evergreen, alternate leaves and whitish flowers in terminal racemes. The fruit is a globular, reddish, berry-like drupe about the size of a pea, with a mealy, insipid pulp. *A. alpina*, growing in the Alpine summits of Maine and New Hampshire, develops a blackish drupe with a juicy and edible pulp. (U. S. Bureau of Plant Industry.)

UVA URSI

Uva Ursi or Bearberry (U. S. P. 1820 to 1936; N. F. 1936 to date) is the dried leaf of *Arctostaphylos Uva-ursi* (Linné) Sprengel or its varieties *coactylis* or *adenotricha* Fernald and MacBride. Both the generic and specific names mean "bear berry," the old Indian name; Greek: *Arctos,* bear; *staphyle,* bunch of grapes; Latin: *Uva,* grape or berry; *ursi,* bear. The plant is a procumbent evergreen shrub indigenous to Europe, Asia and the northern United States and Canada.

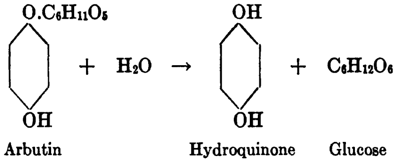
The green leaves only are gathered in the autumn. The commercial supply is largely from the United States and Canada and to some extent from Europe. The leaves are used in Sweden and Russia for tanning "Russia" leather, which receives its aroma from oiling with Oleum Rusci (see page 209). The drug was formerly highly valued in European medicine as an astringent. It was introduced into American medicine about 1800.

Description.—Obovate, spatulate, 12 to 30 mm. in length, 5 to 13 mm. in breadth; summit obtuse; base acute; tapering; margin entire, slightly revolute; upper surface dark green, glabrous, finely reticulate; undersurface yellowish green; petiole about 3 mm. in length, slightly pubescent; texture coriaceous, brittle.

Powder.—Color dusky yellow to light olive; odor slightly aromatic, tea-like; taste astringent, somewhat bitter; epidermal fragments with broadly elliptical stomata and 5 to 8 polygonal, radiate neighbor cells; fragments with spiral tracheæ, narrow, strongly lignified sclerenchymatous fibers, and usually crystal fibers with monoclinic prisms 6 to 30 microns in diameter; pericyclic fibers, lignified, irregular, with thick, porous, tuberculated walls and curved ends; hairs unicellular, non-glandular, short, serpentine or straight; or glandular with a short stalk and a small, one-celled head; numerous fragments of parenchyma that turn bluish black upon the addition of ferric chloride T.S.

Constituents.—Two glucosides, arbutin and ericolin; a crystalline, resinous principle, ursone; tannin, about 5 per cent; gallic acid; ellagic acid; a yellow, crystalline, coloring principle; calcium oxalate; total ash, about 3.25 per cent; acid-insoluble ash, about 0.25 per cent. Ericolin is a yellow, hygroscopic, bitter substance, which yields on hydrolysis the volatile oil, ericinol. Ursone occurs in tasteless needles, insoluble in water but sublimable.

Arbutin is a phenol glucoside which forms colorless, bitter needles and is soluble in water and alcohol, the solutions being colored azure blue upon the addition of an alkali followed by phosphomolybdic acid. Upon hydrolysis, it yields hydroquinone.

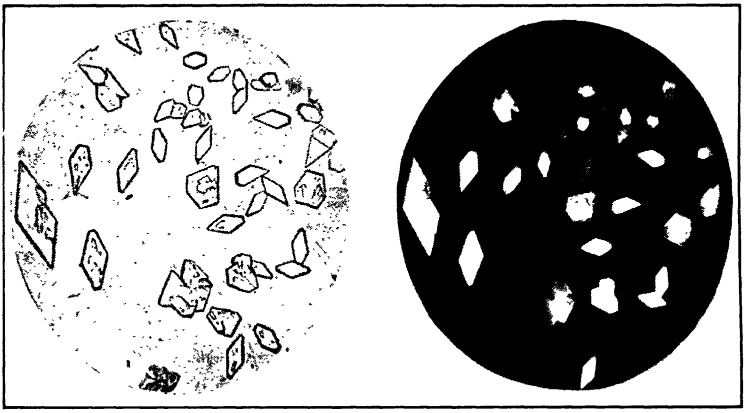


If powdered uva ursi is microsublimed, a sublimate of hydroquinone will readily be formed. **Hydroquinone** is dimorphous, and hexagonal monoclinic plates will occasionally be seen among the feather and rod-like crystals of the sublimate. The crystals polarize light with a brilliant display of colors. Arbutin is localized in the chlorenchyma, and the use of nitric acid colors the cells bright yellow to dark orange, the color gradually fading.

Standards and Tests.—Uva Ursi contains not more than 3.5 per cent of the stems of the plant and not more than 2 per cent of other foreign organic matter, and yields not more than 1.5 per cent of acid-insoluble ash. In sections or in the powder, vanillic acid colors the cells bright red, distinguishing uva ursi from the leaves of *Vaccinium myrtillus.* Sections of leaves of uva ursi are colored bluish black with freshly prepared solutions of ferrous sulfate, distinguishing them from the leaves of *Vaccinium vitis idæa.* Prepare an aqueous extract by boiling 1 gm. of powdered uva ursi in 10 cc. of water; cool, filter and add a few drops of ferrous sulfate T.S.: a grayish purple precipitate is formed.

USES AND DOSE.—Uva Ursi is an astringent, a tonic and a diuretic. Average dose, 2 gm.

ALLIED PLANTS.—Various other species of *Arctostaphylos* contain principles similar to uva ursi. The leaves of **Trailing Arbutus** (*Epigæa repens*) contain ericolin and possibly arbutin. Ericolin occurs in a number of species of *Ledum* and *Rhododendron* and also in **European Huckleberry** (*Vaccinium myrtillus*), a small cranberry (*Vaccinium oxycoccus*) and **Heather** (*Calluna vulgaris*).



A *B*

FIG. 262.—Hydroquinone sublimed from Uva Ursi. *A*, In normal transmitted light; *B*, in polarized light.

A number of species of *Rhododendron* contain, in addition to andromedotoxin, the same principles as found in uva ursi. **Marsh tea** or narrow-leaved **Labrador tea** (*Ledum palustre*), growing in the northeastern United States and Canada, as well as northern Europe and Asia, contains ericolin, arbutin, an ethereal oil (the principal component of which is Ledum camphor), valeric, acetic and butyric acids.

The leaves of *Empetrum nigrum* contain resin, benzoic acid, tannin, a wax, fructose and probably rutin.

Chimaphila or Pipsissewa (U. S. P. 1820 to 1916; N. F. 1916 to 1947) is the dried leaf of *Chimaphila umbellata* (Linné) Barton. *Chimaphila* is from two Greek words meaning winter loving, in allusion to the leaves, green in winter; *umbellata* refers to the flower cluster; Pipsissewa is the American-Indian name for the plant.

The plant is a low perennial herb indigenous to the United States and southern Canada, northern Europe and Siberia. The commercial supplies come mostly from Michigan, Virginia and North Carolina. The North American Indians considered Chimaphila an important medicine.

DESCRIPTION, STRUCTURE AND POWDER.—See Figure 263 and the National Formulary, Seventh Edition.

The drug contains chimaphilin, occurring in golden yellow needles; two glucosides, arbutin and ericolin (see Uva Ursi); several other crystalline principles; a volatile oil; tannin, 4 to 5 per cent. Total ash about 4 per cent with about 0.25 per cent of acid-insoluble ash. Since arbutin is present, hydroquinone may be microsublimed from powdered chimaphila, and identified by the usual microchemical tests.

Chimaphila is an astringent, a tonic and a diuretic. Average dose, 2 gm.

Pyrola Maculata, Chimaphila Maculata or Spotted Wintergreen (U. S. P. 1831 to 1842) resembles in plant characteristics, constituents and medical properties the drug Chimaphila to which, botanically, it is closely related. The leaves of *C. maculata* have lighter irregular spots on the dark green upper surface.

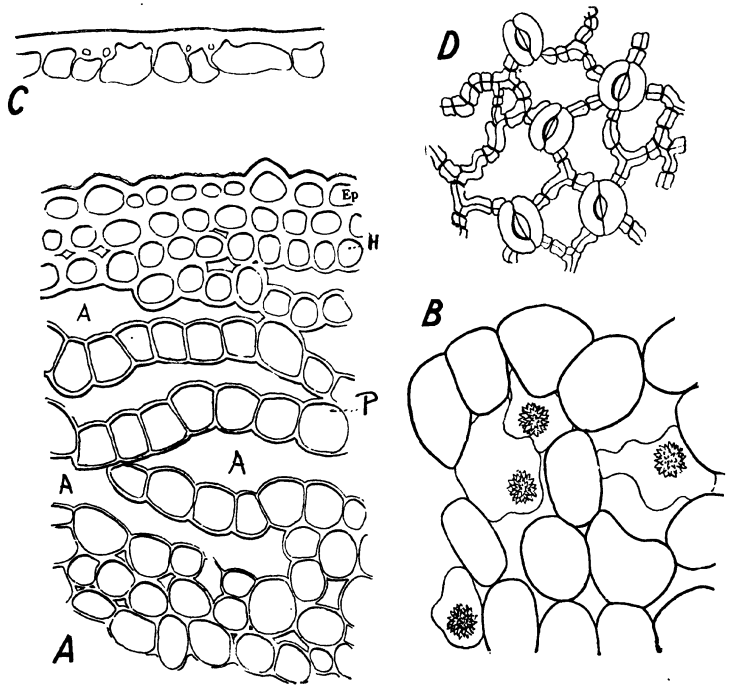


FIG. 263.—*Chimaphila umbellata:* *A*, transverse section of an aërial internode; *Ep*, thick-walled, somewhat papillose epidermal cells; *H*, hypodermis composed of thick-walled collenchymatous cells; *P*, cortex of parenchyma traversed by very wide air-spaces (*A*), due to the separation of the cells in several of the middle layers. The parenchyma contains chloroplastids which are not here shown; and in the air-spaces in alcoholic material there are usually numerous sphæro-crystals. *B*, Transverse section of a portion of the pith of an internode, showing the moderately thickened parenchyma, intermixed with very thin-walled, irregular cells, which contain rosette aggregates of calcium oxalate. *C*, Transverse section of the ventral epidermis showing the heavily thickened outer walls. *D*, Surface view of the dorsal epidermis showing the thick, porous walls of the epidermis cells, and the characteristic stomata which lack neighbor cells. The guard cells of the stomata are slightly raised above the surrounding epidermis, and the wide air-chambers are very shallow. (After Holm.)

Gaultheria, Wintergreen, Teaberry or Checker-berry (U. S. P. 1820 to 1894) consists of the dried leaves of *Gaultheria procumbens*, a low shrub-like perennial, producing slender creeping or subterranean stems, the branches ascending and from 5 to 15 cm. in height. The leaves are alternate and evergreen, the flowers are white and axillary and the fruit is a bright red, globular, aromatic berry. The plant is very common in coniferous woods throughout the eastern United States and Canada. The leaves are coriaceous, the upper surface dark green and shining and the under surface pale green. The odor is distinct, aromatic and the taste aromatic and astringent. For the structure see Figure 264.

Oleum Gaultheriæ, Oil of Wintergreen or Methyl Salicylate (U. S. P. 1820 to date) is obtained from *Gaultheria* plants by steam distillation. The yield from the dry leaves ranges from 0.5 to 1 per cent.

Methyl salicylate, the chief ingredient of this oil, is formed when the glucoside, gaultherin, is hydrolyzed by the naturally occurring enzyme, gaultherase, in the presence of water. Oil of wintergreen also contains (a total of about 1 per cent) triacontane, an aldehyde or ketone having an odor like enanthic or heptyl aldehyde; enanthic alcohol; an ester which splits up into enanthic alcohol and an acid resulting by oxidation from enanthic ketone. Enanthic alcohol and its ester possess the characteristic odor which distinguishes true oil of gaultheria from the artificial methyl salicylate.

The oil is distilled in several eastern states from the wintergreen plants, chopped into small pieces and allowed to stand in water for about twelve hours; it may be purified by rectification. For Standards and Tests see Methyl Salicylate, U. S. Pharmacopœia.

Owing to the demand for this oil and its high price, as compared with artificial methyl salicylate, it may be substituted by oil of birch or the artificial methyl salicylate.

Gaultheria is a stimulant, a diuretic and an astringent.

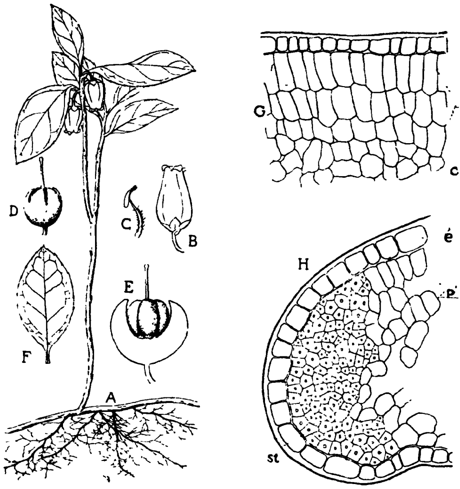


FIG. 264.—*Gaultheria procumbens:* *A*, entire plant showing horizontally creeping stolons and solitary axillary flowers; *B*, flower showing hypocrateriform corolla; *C*, stamen; *D*, young fruit; *E*, section of fruit showing the baccate or berry-like calyx which encloses the true fruit or capsule; *F*, leaf showing venation; *G*, cross-section of leaf showing epidermis (*e*), three layers of palisade cells (*p*), and chlorenchyma (*c*); *H*, cross-section of margin of leaf showing in addition a large group of sclerenchymatous fibers. (After Holm.)

Methyl Salicylate, Gaultheria Oil, Wintergreen Oil, Betula Oil or Oil of Sweet Birch (U. S. P. 1894 to date) is produced synthetically or is obtained by maceration and subsequent distillation with steam from the leaves of *Gaultheria procumbens* Linné or from the bark of *Betula lenta* Linné (Fam. *Betulaceæ*). The product must be labelled to indicate whether it is synthetic or distilled from either of the plants mentioned.

The recovery of the oil from gaultheria has been discussed above. When recovered from birch the process is essentially the same. Methyl salicylate is made synthetically by distilling a mixture of salicylic acid and methyl alcohol.

DESCRIPTION.—Methyl salicylate is a colorless, yellowish, or reddish liquid having the characteristic odor and taste of gaultheria. Consult the U. S. Pharmacopœia for its physical and chemical constants.

CONSTITUENTS.—The principal constituent is methyl salicylate. Oils from natural sources contain small quantities of other constituents, those from gaultheria being discussed above.

USES AND DOSE.—Methyl salicylate is an antiseptic, an antirheumatic and a flavor. Average dose, 0.75 cc.

Statice or Marsh Rosemary (U. S. P. 1820 to 1882) is the root of *Statice Limonium* Linné, var. *caroliniana* Gray (*Limonium carolinianum* (Walt.) Britton (Fam. *Plumbaginaceæ*). The plant is perennial, acaulescent, preferring salty marshes in southern and western Europe.

The root is fleshy, several-headed, branching, deep brownish purple externally, lighter colored internally, and strongly astringent and bitterish in taste. The dry root contains up to 18 per cent of tannin.

The drug has been used orally as a hemostatic, an antidysenteric, and as a gargle for ulcerated throat.

SAPOTACEÆ, OR GUTTA PERCHA FAMILY

This is a family of about 40 genera and 600 species of tropical trees and shrubs. The leaves are alternate and evergreen, the flowers are regular and bisexual and occur in the axils of the leaves; the fruits are berries. The plants are especially characterized by the presence of laticiferous sacs, which occur in rows and are distributed in the pith and cortex and accompany the vascular bundles throughout the veins of the leaves. The latex is composed of irregular doubly refracting, amorphous masses of caoutchouc, which when collected and dried furnishes the gutta percha of commerce. To this family also belongs *Achras sapota,* known as the sapodilla tree or "bully-tree," which is indigenous to tropical America and furnishes the sapodilla plum. The latter resembles a russet apple in color and size, and possesses a milky, acrid juice which disappears when the fruit matures. The fruit then develops a sweet taste and becomes edible. The seeds of the sapodilla are sometimes used in medicine, and the latex obtained from the tree is used in the manufacture of a chewing gum.

Gutta Percha, Gutta Pertscha or Gummi Plasticum (U. S. P. 1863 to 1894; N. F. 1916 to 1926) is the purified, coagulated, milky exudate of several species of *Palaquim* and of *Payena*, evergreen trees indigenous to Indo-China and the East Indies. Usually the tree is felled and circular incisions about 20 cm. apart are made through the bark the whole length of the trunk; the milky juice slowly exudes, hardens on exposure and is collected. The yield per tree is 3 to 5 kg. and may attain 10 kg. The hard exudate is softened in hot water, kneaded, and grosser impurities removed. It is shipped in large blocks weighing about 20 kg.

Purified gutta percha is in flattened pieces, sticks or masses of variable sizes; it is hard, rather leathery, somewhat flexible, elastic, and sinking in water; at 65° C., it becomes plastic; at 100° C. (boiling water) it is soft and capable of being kneaded though assuming its original form on cooling. Externally it is yellowish, grayish brown or dark brown, porous, somewhat fibrous and may be readily cut with a knife; internally it is a grayish white to reddish yellow, frequently with reddish brown streaks of darker colored material; odor slight and somewhat unpleasant.

Gutta percha is usually preserved under water, as when exposed to the air it becomes brittle. It is insoluble in water, cold alcohol, dilute acids and dilute solutions of the alkalis. About 90 per cent is soluble in chloroform, carbon tetrachloride, carbon disulfide, petroleum ether or oil of turpentine. It is partly soluble in boiling alcohol, or boiling ether, and the filtrate, on cooling and evaporating, leaves a crystalline residue. Sulfuric or nitric acids slowly dissolves it.

Gutta percha contains from 80 to 85 per cent of an amorphous hydrocarbon, gutta, which is soluble in chloroform, ether, petroleum ether, paraffin oil, fixed and volatile oils. Two oxidation products of gutta occur in gutta percha, viz., (*a*) alban, from 4 to 16 per cent, a whitish, amorphous resin, soluble in hot alcohol; (*b*) fluavil, from 4 to 6 per cent, a yellowish amorphous resin, soluble in cold alcohol. Total ash, from 0.6 to 1.65 per cent.

Gutta percha is a protective, used for external applications.

It is used in dentistry as a temporary filling for cavities.

Chicle or Sapodilla Gum is the dried latex of *Achras sapota,* a tall evergreen tree cultivated in tropical America. The trunk of the tree is tapped and the dried latex scraped off and exported as crude chicle. This is washed with alkali and after subsequent neutralizing and washing forms the base used in the manufacture of chewing gum.

Balata is the dried latex obtained from *Mimusops balata,* a tree indigenous to the West Indies and South America. Balata possess the general properties of chicle and is employed in the manufacture of "bubble gum."

Diospyros or Persimmon (U. S. P. 1820 to 1882) is the unripe fruit of *Diospyros virginiana* Linné (Fam. *Ebenonaceæ*), a tree indigenous to eastern United States. The fruit ripens in November, but should be gathered as a drug in October while still green. It is very astringent with tannin, and medicinally is used as an astringent. Average dose, 2 gm. The ripe fruit contains malic acid and sugar and is edible. It is used in bread and cakes, and is fermented to form a beer.

STYRACACEÆ, OR STYRAX FAMILY

This is a small family of 8 genera and 120 species of trees and shrubs, mostly indigenous to tropical South America, a few representatives being found in the southern United States. The leaves are mostly simple and alternate; the flowers are regular and either in axillary clusters or racemes and the fruit is either a berry, a drupe or a capsule. Very many of the plants contain a benzoic resin. This occurs in lysigenous, intercellular secretory receptacles, which develop in the wood and bark as a result of certain pathological phenomena. Among special histological characters the following are of some importance: The cork originates either in or below the pericycle, the latter usually containing isolated groups of bast fibers. The stomata on the leaves are usually unaccompanied by neighbor cells, although when present they are parallel to the pore. Non-glandular hairs are either stellate or in the form of peltate scales. Glandular hairs are wanting.

BENZOIN

Benzoin or Gum Benjamin (U. S. P. 1820 to date) is the balsamic resin obtained from *Styrax benzoin* Dryander, known in commerce as Sumatra Benzoin (U. S. P. 1820 to date), or from *Styrax tonkinensis* (Pierre) Craib et Hartwich, or other species of the Section *Anthostyrax* of the genus *Styrax,* known in commerce as Siam Benzoin (U. S. P. 1905 to date). *Styrax* is the ancient Greek name of storax, the name applied to a sweet-scented gum and to the tree producing it; benzoin is from the Arabic word *ben,* "fragrant," or the Hebrew *ben,* "a branch" and *zoa,* "an exudation," meaning "the juice of the branch;" *tonkinensis* is after Tonkin, a state in French Indo-China.

The plants are trees of medium height growing in southeastern Asia and the East Indies. *S. benzoin* is cultivated throughout Sumatra; *S. tonkinensis* in Siam, north Annam and Tonkin. Benzoin is a pathological product developed by incising the bark. After about two months the exuding balsamic-resin becomes less sticky and hard enough to be collected. In Sumatra the collected resin is pressed into tins lined with linen and then removed in blocks. In Siam the separate tears are scraped from the trees. New incisions are continually made until the trees die. The tree contains no secretory cells, nor does it contain the constituents of the balsamic resin, until it is incised. The bark of the normal tree contains considerable tannin; probably the resinotannols in benzoin are produced from this tannin. Benzoin was unknown to the Greeks and Romans. Its first mention was that of Ibn Batuta who visited Sumatra in the fourteenth century. In the fifteenth century it still appears as a precious balsam but in the sixteenth century it is an article of Venetian commerce.

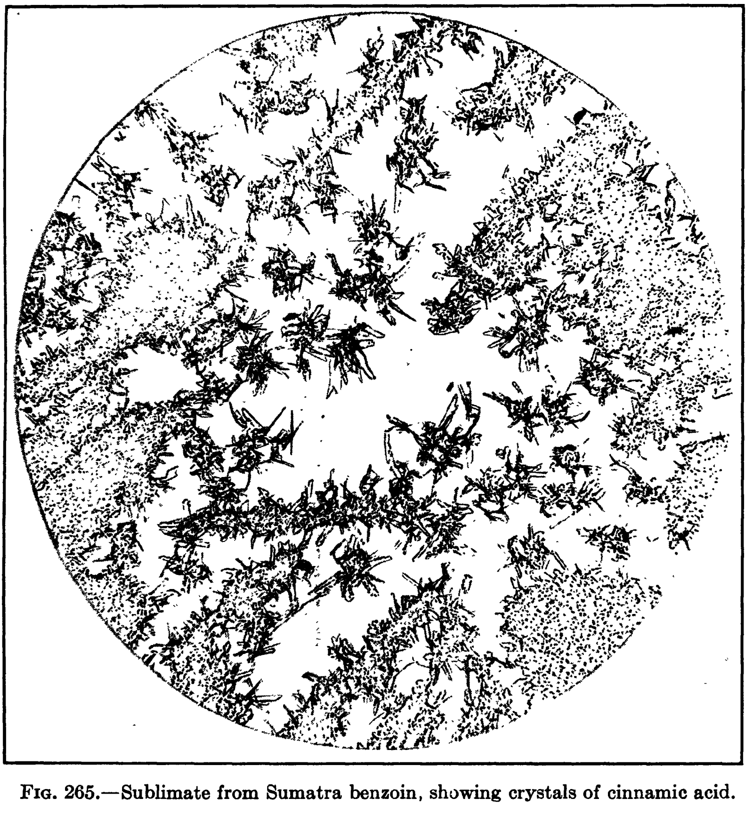


FIG. 265.—Sublimate from Sumatra benzoin, showing crystals of cinnamic acid.

DESCRIPTION.—Sumatra benzoin is in blocks or irregular masses composed of tears of variable size imbedded in a translucent or opaque matrix; brittle; the tears internally milky white, becoming soft on warming and gritty when chewed; the matrix reddish or grayish brown; odor agreeable, balsamic, resembling that of styrax; taste aromatic, resinous.

Siam benzoin occurs mostly in separate concavo-convex tears, yellowish brown to rusty brown externally and milky white on the freshly broken surface, brittle but becoming soft upon warming and plastic on chewing; it has a vanilla-like odor.

CONSTITUENTS.—Sumatra benzoin contains about 75 per cent of a resinous substance, benzoresin, which consists of: (*a*) an ester of cinnamic acid and resinotannol (92.6 per cent), and (*b*) an ester of cinnamic acid and benzoresinol. Benzoresin on decomposition yields 30.3 per cent of cinnamic acid; 64.5 per cent of resinotannol, which is soluble in a concentrated sodium salicylate solution and 5.2 per cent of benzoresinol. Sumatra benzoin contains about 17 per cent (10 per cent free) cinnamic acid and about 9 per cent (6 per cent free) benzoic acid, traces of benzaldehyde and benzol; 0.1 to 1 per cent of vanillin; 1 per cent of the phenylpropyl ester of cinnamic acid; 2 to 3 per cent of styracin (cinnamic cinnamate); and 14 to 17 per cent of insoluble matter, consisting chiefly of woody tissues.

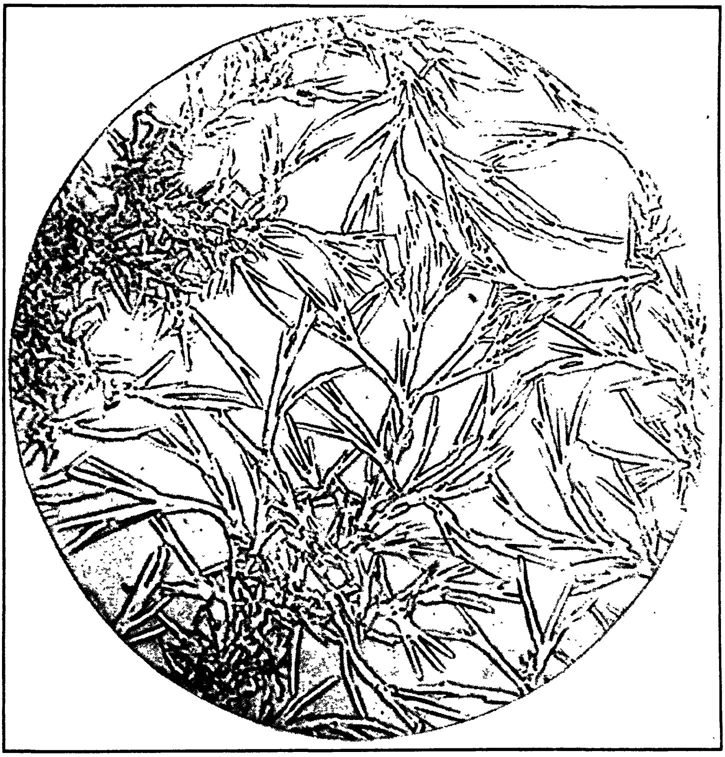


FIG. 266.—Sublimate from Siam benzoin showing crystals of benzoic acid.

Siam benzoin consists largely of a resinous substance, siabenzoresin, composed of about 90 per cent of an ester of benzoic acid and siaresinotannol and about 10 per cent of an ester of benzoic acid and benzoresinol. Siabenzoresin on saponification yields 38.2 per cent of benzoic acid, 56.7 per cent of siaresinotannol and 5.1 per cent of benzoresinol. Siam benzoin also contains about

12 per cent of free benzoic acid; very little or no cinnamic acid; 0.3 per cent of a neutral aromatic liquid; 0.15 to 1.5 per cent of vanillin; and 1.3 to 3.3 per cent of impurities in the form of woody tissues. **Penang benzoin** has an odor of storax and in composition resembles Siam benzoin. It contains considerable benzoic acid, and it and **Palembang benzoin,** produced in Sumatra, are a source of benzoic acid.

STANDARDS AND TESTS.—Sumatra benzoin yields not less than 75 per cent of alcohol-soluble extractive and not more than 1 per cent of acid-insoluble ash. Siam benzoin contains not more than 1 per cent of foreign organic matter and yields not less than 90 per cent of alcohol-soluble extractive and not more than 0.5 per cent of acid-insoluble ash.

Warm about 0.5 gm. of coarsely powdered benzoin in a test-tube with 10 cc. of potassium permanganate T.S. With Sumatra benzoin the odor of benzaldehyde is evolved, due to the oxidation of cinnamic acid, but with Siam benzoin no benzaldehyde odor is perceptible.

When 2 or 3 drops of sulfuric acid are added to an ethereal solution of benzoin in a porcelain dish, that of Sumatra benzoin produces a deep red-brown coloration while that of Siam benzoin produces a deep purplish red coloration.

Siam benzoin yields not less than 12.5 per cent of residue to warm carbon disulfide. The residue responds to the customary tests for benzoic acid. Benzoin does not show the presence of rosin.

When microsublimed in the usual way Sumatra benzoin yields a sublimate of plates and small rods (cinnamic acid) which strongly polarize light, while Siam benzoin yields a sublimate of needles and rod-shaped crystals (benzoic acid) which do not strongly polarize light.

USES AND DOSE.—Benzoin is an antiseptic, a stimulant, an expectorant and a diuretic.

Benzoic Acid ($HC_7H_5O_2$) (U. S. P. 1820 to date) is now mostly a synthetic product, but was first obtained by sublimation from Sumatra benzoin.

It occurs as white crystals, usually as scales or needles. It has a slight odor of benzoin and is volatile at moderate temperatures, and freely so in steam. It is readily soluble in the usual organic solvents, but requires 275 parts of cool water for solution. It readily forms salts with alkalis.

Benzoic acid and its sodium salt have an extensive use as a preservative of foods, drinks, fats, pharmaceutical preparations, etc. Medicinally it is used as a mild antiseptic, stimulant expectorant, and in certain genito-urinary diseases; externally, as wound dressing. Average dose, 0.5 gm. It is extensively used in veterinary practice as an expectorant and antipyretic.

MICROCHEMISTRY OF THE BALSAMS

Balsams are resinous substances containing appreciable amounts of benzoic or cinnamic acid. Benzoic acid may be readily sublimed from balsam of Peru, balsam of Tolu and benzoin, while cinnamic acid is readily sublimable from balsam of Peru, balsam of Tolu, storax and Sumatra benzoin. When both acids are present both will be obtained in the sublimate and the following rules are suggested for their differentiation: (1) Benzoic acid usually appears in the sublimate first, the cinnamic acid appearing later; (2) cinnamic acid is more readily soluble in water than benzoic acid; (3) the crystals of cinnamic acid (and its esters) polarize light with a brilliant display of colors while benzoic acid appears gray; (4) the crystals of cinnamic acid are more perfectly formed than those of benzoic acid; (5) benzoic acid will completely volatilize from the preparation within a few days at room temperature; (6) upon the addition of silver nitrate solution the crystals of cinnamic acid (and its ester) become brown, lose their property of polarizing light and for the most part go into solution (the crystals of benzoic acid also dissolve but appear later as crystals of silver benzoate which polarize light well); (7) if the sublimate of cinnamic acid is subjected to bromine vapors for one-half hour the crystals change to yellowish brown drops while crystals of benzoic acid only partially dissolve and remain colorless. If a drop of carbon disulfide is added to the cinnamic acid slide and covered with a cover glass, plates of dibromcinnamic acid will appear; (8) if the sublimate is treated with a drop of potassium permanganate solution and warmed, benzaldehyde is formed which may be detected by its odor.

OLEACEÆ, OR OLIVE FAMILY

This is a family of about 22 genera and 500 species of trees and shrubs of wide distribution, and well represented in the United States. The leaves are opposite and exstipulate, being either simple or odd-pinnate; the flowers are 2- to 4-parted and are usually in panicles; the fruit is either a samara, drupe or berry; the fibrovascular bundles are of the bicollateral type; the non-glandular hairs are usually peltate; calcium oxalate is secreted in the form of small acicular or prismatic crystals; the tracheæ usually possess simple pores only; in the mesophyll of the leaves, sclerenchymatous fibers or spicular cells are frequently developed.

OLIVE OIL

Olive Oil or Sweet Oil (U. S. P. 1820 to date) is the fixed oil obtained from the ripe fruit of *Olea europæa* Linné. The generic name *Olea* is from *oliva,* the Latin name of the olive or from *elaion,* the Greek word meaning oil.

The olive tree is a small evergreen tree attaining a great age but seldom exceeds 10 meters in height. It is apparently a native of Palestine and has been widely cultivated in the Mediterranean countries from remote antiquity. It is now also cultivated for its edible fruit and the oil it yields, in southwestern United States and many other subtropical localities. There are a large number of cultivated varieties of the olive, the fruits of which vary widely in size, color when ripe, and in yield of oil.

The olive tree was known in Egypt in the seventeenth century B.C. Its branches have long been used as an emblem of peace. The fruit and its oil were known to the ancient Hebrews and are frequently mentioned in the Old Testament. The olive was introduced into Spain at an early date.

The fruit is a drupe and when ripe, usually is purplish in color. The full grown, but green fruit, as well as the ripe fruit, when pickled in brine, are widely used as a condiment. The olive "stone" or endocarp enclosing the seed has been finely comminuted and used as an adulterant of spices and certain powdered drugs (see Fig. 88). Olive wood is highly prized for cabinet work.

Olive oil is of several grades of purity: Virgin oil is obtained by gently pressing the peeled pulp freed from the endocarp; it is rarely exported. First and second grades of edible oil are pressed from crushed pulp, the first grade with less pressure, the second grade from the same pulp with more pressure. Handpicked olives are used and the oil is obtained promptly before decomposition produces fatty acids. Finally the pulp, mixed with hot water, is pressed again for technical oil; or the pulp is extracted with carbon disulfide to obtain "sulfur" olive oil, of inferior quality. The fallen, decomposed or refuse olives, allowed to ferment, furnish "Tournant Oil," which contains large amounts of free fatty acids, and is used as "turkey-red oil."

DESCRIPTION.—A pale yellow or pale greenish yellow oily liquid; odor slight; characteristic; taste bland, becoming faintly acrid. Olive oil is miscible with ether, carbon disulfide and chloroform; slightly soluble in alcohol. Specific gravity, 0.910 to 0.915 at 25° C. Upon chilling it tends to become cloudy and at 0° C. it usually forms a whitish granular mass.

CONSTITUENTS.—Olive oil consists chiefly of olein. It also contains linolein, palmitin and arachin, the latter frequently separating when the oil is chilled.

STANDARDS.—Olive oil should be free from cottonseed oil, peanut oil, sesame oil, and tea-seed oil. Consult the U. S. Pharmacopœia for their detection.

USES AND DOSE.—Olive oil is a nutrient, a demulcent, a laxative and an emollient. Average dose, 30 cc. It is employed pharmaceutically in the preparation of soaps, plasters, etc., and is widely used as a salad oil.

The leaves of the olive tree were employed many years ago as a remedy in intermittent fever and quite recently attention has again been directed to their therapeutic value as a tonic and febrifuge.

Manna (U. S. P. 1820 to 1936; N. F. 1936 to 1947) is the dried exudation of *Fraxinus ornus* Linné, yielding not less than 75 per cent of anhydrous extractive soluble in boiling alcohol. *Manna* is from the Hebrew *man*, meaning a gift from Heaven; *fraxinus* is Greek meaning to fence in, and refers to the plants being used for hedges or fences; *ornus* is the Latin name for the wild mountain ash.

The plant is a small tree indigenous to southern Europe, where it is also cultivated, particularly in Sicily. Manna is obtained from incisions in the bark of trees about eight years old. The exudation hardens on the bark, or is collected in special receptacles. Large Flake manna consists of light-colored pieces 10 to 20 cm. in length; Small Flake manna is in smaller, light yellowish brown pieces; "Sorts" consists of small agglutinated tears and fragments of the flakes, brownish, sticky, only slightly crystalline, and very inferior in quality. Large Flake manna is preferred.

The name manna has been applied to a number of saccharine exudations obtained from different plant species and of varying composition. The manna of the Scriptures may have been an edible lichen used by the Israelites as a food during their journey through the wilderness of Arabia. The manna from the manna ash came into use in Europe during the fifteenth century; before that the manna used came from the East.

DESCRIPTION.—In irregular, 3-sided, more or less elongated pieces, one side being smooth and concave; externally yellowish white; friable, somewhat waxy; internally whitish, porous and crystalline with not less than 40 per cent of brittle or soft, yellowish white or yellowish gray fragments or tears; odor suggestive of maple sugar; taste sweet, slightly bitter and acrid.

The drug contains mannitol, 50 to 60 per cent; fraxin, a green-fluorescent glucosidal principle, in bitter, colorless prisms that are soluble in water and alcohol; mannose, in two forms, mannotriose (a trisaccharide), 6 to 16 per cent of manna, and mannotetrose (a tetrasaccharide), 12 to 16 per cent; mucilage; resin; total ash, 0.85 per cent; acid-insoluble, 0.05 per cent. Manna is a laxative. Average dose, 15 gm.

ALLIED PRODUCTS.—A number of other species of *Fraxinus* indigenous to Europe also yield manna, though inferior to the official kind.

The leaves of a number of species of *Eucalyptus* (Fam. *Myrtaceæ*) secrete a manna-like carbohydrate, as *E. gunnii* and *E. resinifera*.

Mannitol or Mannite (N. F. 1936 to date) is a hexyhydric alcohol, $C_6H_8(OH)_6$, obtained by the reduction of mannose or by isolation from manna. It crystallizes in orthorhombic prisms or in aggregates of fine needles (see Fig. 267); it is freely soluble in water and boiling alcohol, but almost insoluble in cold alcohol. For constants and tests of purity, see the National Formulary, Reagent Section. Mannitol is a nutritive used by diabetics; apparently it forms no glucose in the blood. It is also used in certain bacteriological culture media.

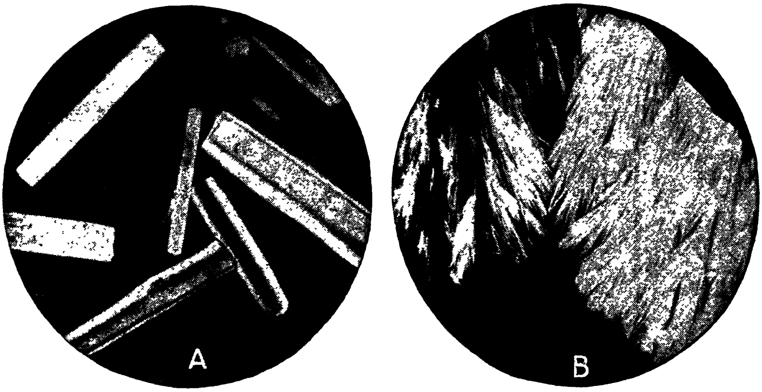


FIG. 267.—Orthorhombic crystals of Mannitol (Mannite) obtained from aqueous solutions: *A*, large crystals; *B*, feathery aggregates of needles.

Chionanthus or Fringe Tree Bark (N. F. 1916 to 1947) is the dried bark of the root of *Chionanthus virginicus* Linné. *Chionanthus* is from two Greek words, meaning snow and flower, in reference to the snow-white clusters of flowers. The plant is a tall shrub, indigenous to the southern United States and extensively cultivated, with deep green, glossy foliage and delicate flowers which hang in loose, drooping, graceful panicles. When grafted on certain species of *Fraxinus*, it becomes more vigorous and attains a height of 8 or 9 meters. The eclectic extract prepared from the recently gathered bark has been extensively used in medicine.

The drug occurs in transversely curved pieces or in quills, the bark from 2 to 10 mm. in thickness; hard and heavy; outer surface reddish brown, occasionally grayish; rough, scaly, occasionally with numerous lenticels and irregular scars; inner surface weak yellowish orange, distinctly striate; fracture short, hard and granular.

The cork consists of tangentially elongated cells with lignified walls, but no stone cells; the cortical parenchyma contains numerous starch grains and a few small prisms, and is associated with a few groups of stone cells and fibers; the inner bark is of small parenchyma cells, sieve tissue, and nearly straight tapering medullary rays, 1 to 3 cells wide.

The powder is weak yellowish orange in color with a distinctive odor and a very bitter taste; it contains large stone cells, the walls thick, non-striated, strongly lignified and porous; a few short blunt fibers from the bark at the base of the stem with very thick, porous, lamellated, lignified walls; starch grains simple and compound, 3 to 27 microns in diameter, spheroidal, reniform, plano-convex or polyhedral in shape.

Chionanthus yields not less than 35 per cent of anhydrous extractive soluble in 73 per cent alcohol.

Chionanthus is an alterative and a tonic. Average dose, 2 gm.

Fraxinus or White Ash Bark (N. F. 1916 to 1926) is the bark of *Fraxinus americana*, a large, beautiful forest tree of the northern United States and Canada. The bark is collected in the spring, from the branches, trunks and roots of trees from ten to twenty-five years of age. The outer periderm should be removed. The root bark is preferred. It occurs in nearly flat pieces 3 to 10 mm. in thickness; outer surface reddish brown, irregularly furrowed and with numerous shallow patches, frequently with the yellowish gray outer periderm present; inner surface yellowish brown, nearly smooth, somewhat longitudinally striate; fracture uneven, short-fibrous; odor slight, aromatic; taste bitter, slightly aromatic and acrid.

Fraxinus contains a volatile oil; an alkaloid; several resins; starch and sugar; neither tannic nor gallic acid apparently is present. Total ash about 4.25 per cent, with 0.25 per cent of acid-insoluble ash.

The bark of *Fraxinus excelsior*, a tree growing in Europe and Northern Asia, is used in European countries. It is collected in Spring from young twigs, forms quills upon drying and is 2 to 3 mm. in thickness. Externally it is grayish or grayish green, somewhat scaly; the inner surface light yellowish; the fracture is fibrous; taste bitter and astringent. It contains a crystalline glucoside, fraxin; a crystalline bitter principle, fraxinin; and tannic acid from 2 to 3 per cent.

LOGANIACEÆ, OR NUX VOMICA FAMILY

This is a family of 33 genera and about 600 species, which are widely distributed. The plants are variable in character, ranging from annual herbs to trees, some being twining and woody vines. The leaves are simple, the flowers regular, having tubular or somewhat campanulate corollas, and the fruit is either a berry or a capsule. The cork is frequently lamellated. There is usually a ring of stone cells in the primary cortex, as in certain species of *Strychnos*. The tracheæ possess simple pores or scalariform perforations, except when the walls are in contact with the cells of the medullary rays, when they develop bordered pores. Calcium oxalate is secreted in all of the usual forms. In the *Loganioideæ* the non-glandular hairs are either unicellular or uniseriate, those in *Strychnos* having a specific value. In *Spigelia* there are developed stellate hairs composed of single united cells, which are inserted upon a multicellular stalk. True glandular hairs, having flattened heads, are only found in *Buddleioideæ*.

NUX VOMICA

Nux Vomica (U. S. P. 1820 to 1947; N. F. 1947 to date) is the dried ripe seed of *Strychnos Nux vomica* Linné. *Strychnos* is the Greek name for a number of poisonous plants; *Nux vomica* is from two Latin words, meaning "a nut that causes vomiting."

The plant is a small tree about 12 meters tall, native to the East Indies and also found in the forests of Ceylon, on the Malabar Coast and in northern Australia. The fruit is a berry with from 3 to 5 seeds, which are freed from the bitter pulp by washing, and dried before exportation. Most of the commercial supplies come from the Madras Presidency. It was introduced into Europe about the Sixteenth century, though it was mainly used for poisoning animals. Its employment in medicine began about 1640. The natives of India apparently had no knowledge of its medical value.

DESCRIPTION.—See Figure 268 and the National Formulary.

STRUCTURE AND POWDER.—See Figures 269, 270 and the National Formulary.

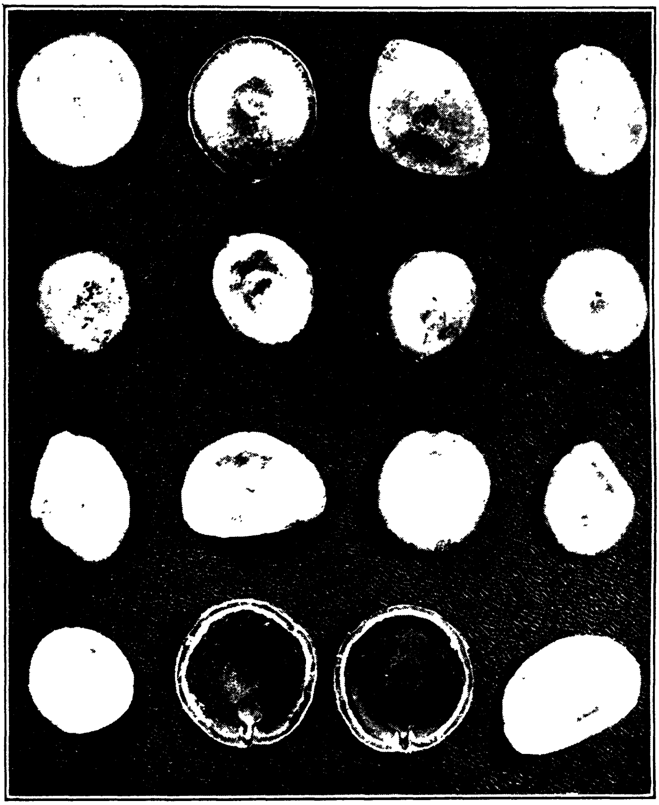


FIG. 268.—Nux Vomica: orbicular, compressed, concavo-convex, sometimes irregularly bent, margin acute or rounded, 10 to 30 mm. in diameter, 3 to 5 mm. in thickness; externally grayish yellow or grayish green, covered with appressed hairs giving the seed a satiny luster, sometimes with adhering dark-brown fragments of the fruit pulp; hilum, near the center of one side and a more or less distinct ridge resembling a raphé extending from it to the micropyle; very hard when dry, tough when damp; internally whitish, horny; endosperm in two more or less regular concavo-convex halves; embryo small, situated near the micropyle, and with two heart-shaped cotyledons; inodorous; taste intensely and peristently bitter. The two halves of the seed at the middle of the bottom row show the two cotyledons and the caulicle of the embryo lying against the endosperm.

CONSTITUENTS.—Natural ash, about 1.5 per cent, soluble in diluted hydrochloric acid; chlorogenic (igasuric) acid, a dibasic acid, crystallizing in needles, its solutions giving a green color with solutions of ferric chloride; 1.5 to 5 per cent of alkaloids consisting of strychnine and brucine, the former comprising from one-third to one-half of the total amount. A glucoside, loganin, is present in the seeds in small amount, but it is found in the pulp of the fruit to the extent of 5 per cent. The alkaloids are probably distributed in both the cell contents and the cell wall. Their presence in the wall is shown by the use of iodine solution and in the contents by the use of potassium dichromate and sulfuric acid.

STANDARDS.—Nux Vomica yields not less than 1.15 per cent of strychnine.

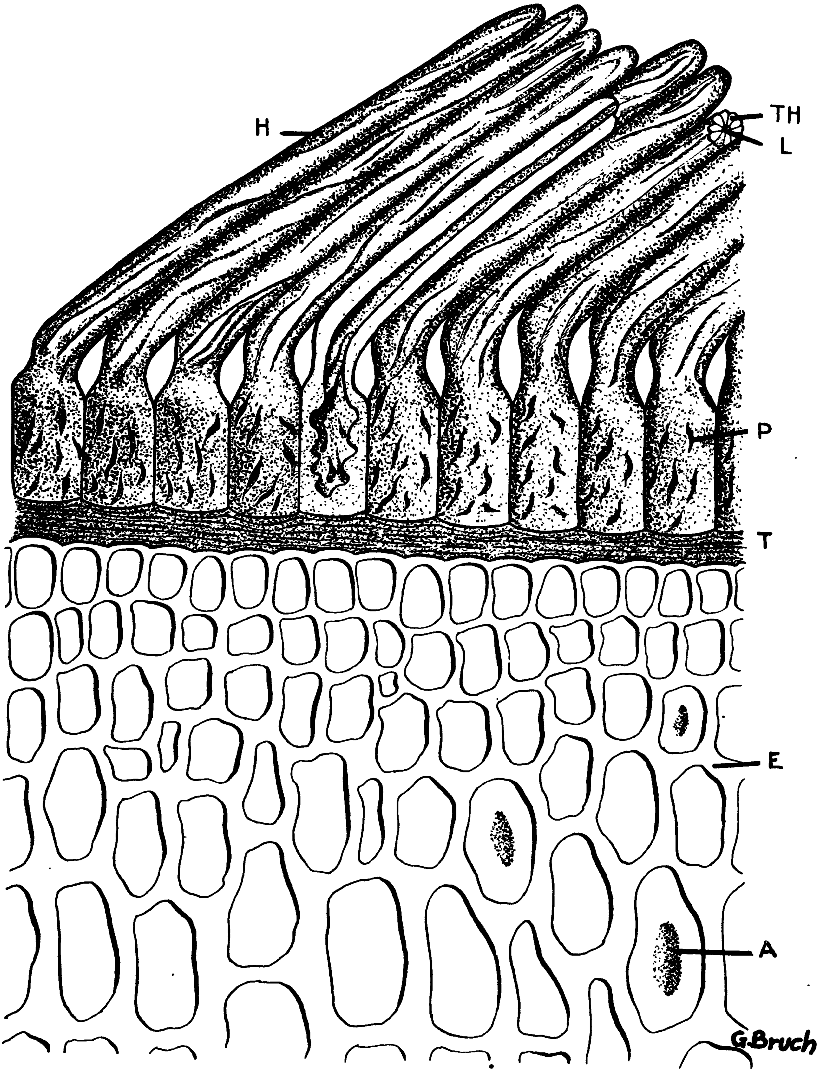


FIG. 239.—Nux Vomica: transverse section through the outer portion of the seed, showing the bent and twisted hairs (*H*) having slit-like pits in the base (*P*) and long curved, very narrow slits in the body of the hair. The fifth hair from the left is shown in longitudinal section. The seventh hair from the left is shown in transverse section indicating the rod-like thickenings in the wall (*TH*) and the circular lumen (*L*). Beneath the hairs are a thin testa (*T*) composed of collapsed cells, and an endosperm (*E*) of cells with thick cellulose walls and containing aleurone, fixed oil and protoplasm (*A*). (Drawing by Gerston Bruch.)

Uses and Dose.—Nux Vomica has a stimulant action upon the central nervous system, especially so upon the spinal cord. It is a motor excitant, a spinant and a tonic. Average dose, 0.1 gm.

Ignatia or Saint Ignatius Bean (U. S. P. 1863 to 1894; N. F. 1916 to 1936) is the dried ripe seed of *Strychnos Ignatii*, a woody climber of the Philippine Islands. *Ignatii* was given in honor of Ignatius, the founder of the Jesuits who introduced the seed of the plant into Europe from the Philippines in 1699. The seeds are irregular, somewhat oblong or ovoid, pebble-like, 20 to 30 mm. in length; grayish or brownish black, more or less translucent and are nearly free from lignified hairs, such as are found in nux vomica.

Ignatia contains about the same amount of total alkaloids as nux vomica, one-third to two-thirds being strychnine. Total ash about 3 per cent, acid-insoluble ash about 0.1 per cent.

Ignatia possesses the same properties as nux vomica.

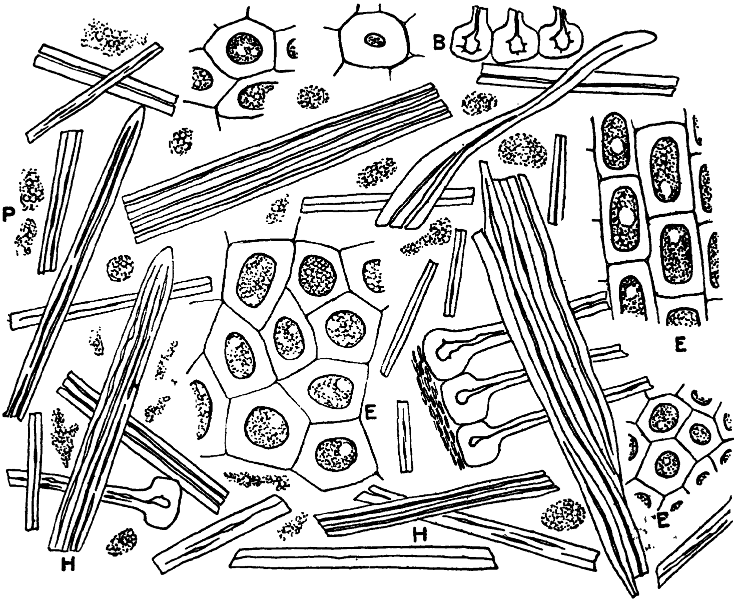


Fig. 270.—Nux Vomica: *H*, fragments of lignified hairs of seed coat; *B*, basal portion of hairs; *E*, thick-walled parenchyma cells of endosperm containing one or more oil globules and protoplasm; *P*, isolated protoplasmic substance from endosperm cells.

Strychnine (U. S. P. 1842 to 1926; N. F. 1926 to date).
Strychnine Sulfate (U. S. P. 1863 to date).
Strychnine Nitrate (U. S. P. 1905 to 1942; N. F. 1942 to date).
Strychnine Phosphate (N. F. 1936 to date).

Strychnine Glycerophosphate (N. F. 1916 to 1926).
Strychnine Valerate (N. F. 1916 to 1926).

Brucine Sulfate (N. F. 1936 to date).

Strychnine and Brucine are usually obtained from nux vomica, but may be obtained from ignatia. The drug is extracted with dilute sulfuric acid; the solution is concentrated; the alkaloids are precipitated with lime, separated by means of solvent, and purified by recrystallization. Brucine is far more soluble in water and in alcohol than is strychnine, though strychnine sulfate is somewhat more soluble in these two solvents than is brucine sulfate.

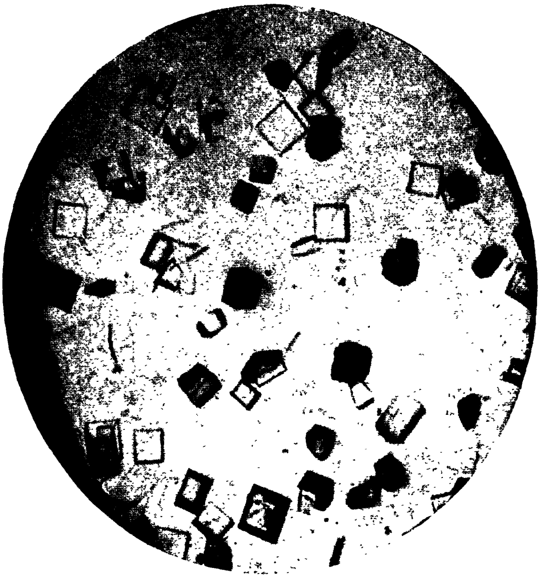


FIG 271.—Strychnine sulfate: tetragonal crystals from aqueous solution, in ordinary light showing basal and side aspects.

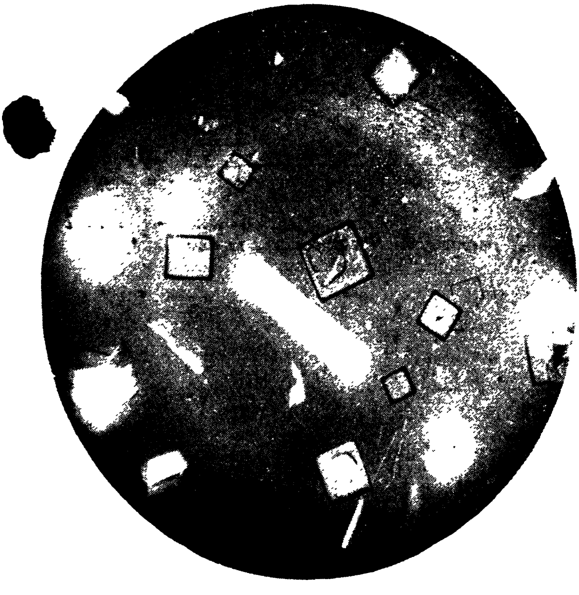


FIG. 272.—Strychnine sulfate: tetragonal crystals from aqueous solution, showing basal aspect in polarized light. Also one large crystal of a second form (orthorhombic?) of strychnine sulfate.

Constants, Solubilities and Tests of Identity and Purity.—Consult the U. S. Pharmacopœia and the National Formulary.

Brucine is always associated in the plant kingdom with strychnine. It contains two methoxyl groups and may be di-methoxy-strychnine. Like strychnine it crystallizes from water in rectangular octahedra, though strychnine also forms tetrahedra.

Brucine is readily distinguished from strychnine by the deep red color it forms with nitric acid, while strychnine assumes but a pale yellow color. Strychnine solution in sulfuric acid, 1 to 20, develops a blue color with a small fragment of potassium dichromate, the color changing to deep violet, purplish red, orange and yellow. Strychnine dissolved in sulfuric acid, containing 1 per cent of ammonium vanadate, forms a deep violet-blue color, changing to deep purple and finally to cherry-red. Brucine interferes with these reactions. Brucine is less active therapeutically than strychnine upon man, but is sometimes preferred in veterinary treatment.

Uses and Dose.—Strychnine and its salts are stimulants to the central nervous system, acting especially on the spinal cord. They are motor excitants, spinants, and bitter tonics. Average dose, strychnine, 1.5 mg.; strychnine sulfate, phosphate or nitrate 2 mg.

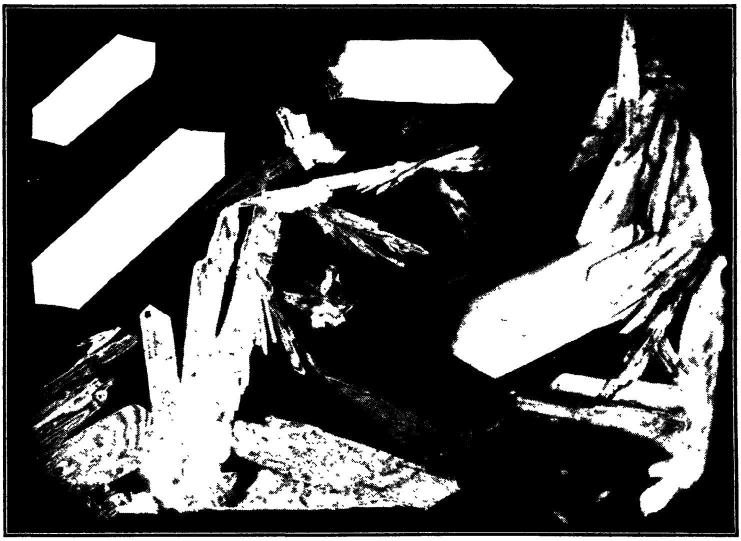


Fig. 273.—Brucine sulfate: orthorhombic crystals from aqueous solution.

Curare or South American Arrow Poison (U. S. P. Reagent 1916 to date) varies in composition among Indian tribes. However, the bark of one or more species of *Strychnos* apparently is always used in its preparation. *Strychnos Castelnæi* Weddell, *S. toxifera* Bentham, *S. Crevauxii* G. Planchon and *Chondodendrom tomentosum* Ruiz et Pavon are commonly employed.

The young bark is scraped off the plants, mixed with other items, boiled in water and strained, or extracted by crude percolation with water, then evaporated to a paste over the fire or in the sun. The imported article is a brownish or black, shiny, resinoid, very bitter mass; readily soluble in cold water and in dilute alcohol.

The drug contains several alkaloids: curarine and protocurarine give the typical effects; curine is devoid of muscle-nerve action, but first stimulates, then depresses the heart action. Curare has a definite paralyzing action on voluntary muscle-nerve endings. Hypodermic injection of a suitable dose causes a total loss of motion, first of the voluntary, then of the respiratory muscles, death resulting from respiratory failure. Therapeutically, the drug is a powerful antispasmodic, used in the convulsions of strychnine poisoning and of tetanus: as an adjunct to shock therapy in neuropsychiatry, and to promote muscular relaxation in surgical anesthesia. It is an important laboratory item for paralyzing the skeletal muscles of test animals.

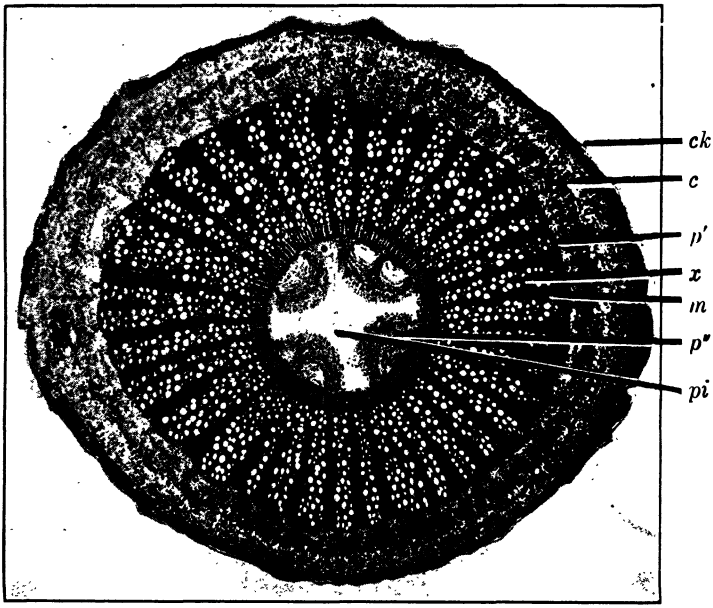


FIG. 274.—*Gelsemium sempervirens.* Transverse section of the rhizome showing a strongly developed cork (*ck*); (*c*) a cortex consisting largely of starch-bearing parenchyma with a few small scattered groups of stone cells or short fibers; (*p'*) crescent-shaped patches of phloem; (*x*) broad xylem wedges, with large tracheæ and thick-walled tracheids; *m*, broad wedge-shaped medullary rays with strongly lignified cells in the xylem region, but non-lignified in the phloem region, the cells containing starch, or especially in the phloem region, prisms of calcium oxalate; four internal phloem patches (*p''*) and a small pith (*pi*). (Photomicrograph by Adamson.)

GELSEMIUM

Gelsemium or Yellow Jasmine Root (U. S. P. 1863 to 1926; N. F. 1926 to date) consists of the dried rhizome and roots of *Gelsemium sempervirens* (Linné) Persoon. *Gelsemium* is from *gelsemino,* the Italian name for jasmine; *sempervirens* is composed of two Latin words, meaning ever-living, alluding to the evergreen character of the plant. The plant is a perennial woody climber growing in the moist woodlands of the southeastern United States. The rhizomes and roots are dug in the autumn, cleaned and dried. Gelsemium came into use about 1821, when its properties were discovered through accident. It was extensively employed by the Eclectics and finally came into general usage in 1870.

Description.—Rhizome horizontal, cylindrical, 3 to 30 mm. in diameter; externally moderate brown with darker purplish lines, longitudinally wrinkled, transversely fissured; upper surface with few stem-scars; under and side portions with occasional roots or root scars; fracture tough, fibrous; internally pale yellowish orange to weak yellow; bark about 1 mm. in thickness; wood distinctly radiate, excentral, with four groups of intraxylary phlœm, pith disintegrated. Roots light brown, 3 to 20 cm. in length, 2 to 8 mm. in thickness; fracture one-half transverse, the other oblique or splintery; internally light yellow; bark about 0.5 mm. in thickness; wood distinctly radiate.

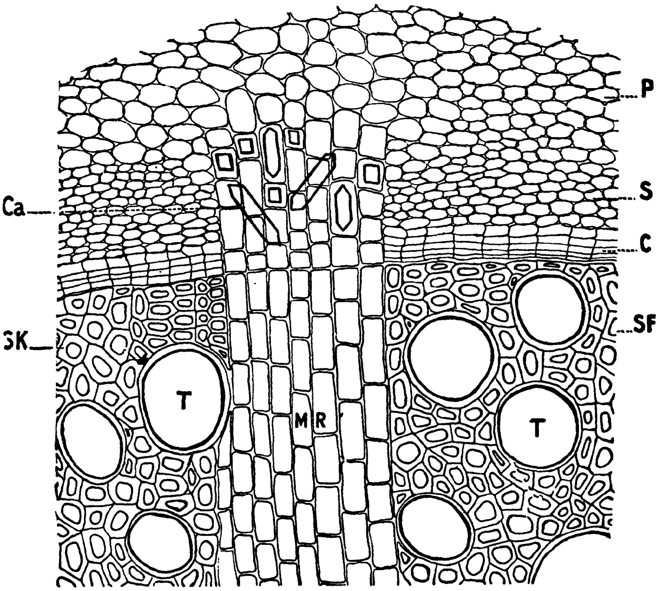


Fig. 275.—Transverse section of gelsemium near the cambium: *P*, parenchyma; *S*, sieve; *C*, cambium; *Ca*, calcium oxalate crystals; *SK*, *SF*, tracheids; *T*, tracheæ; *MR*, medullary ray.

The overground stem is dark or reddish brown and longitudinally wrinkled and has numerous lenticels and a few, somewhat elliptical branch-scars; the bark is about 0.2 mm. in thickness and somewhat greenish.

Structure.—See Figures 274 and 275.

Powder.—Light yellowish brown to weak yellow; cork cells grayish or yellowish brown and more or less lignified; tracheal fragments with conspicuous bordered pores; fiber tracheids long, narrow, lignified; stone cells few, with very thick, porous, strongly lignified walls; starch grains spheroidal, from 4 to 12 microns in diameter; calcium oxalate in long monoclinic prisms, from 15 to 32 microns in diameter. In the powder of the overground stem, collenchymatous cells containing chloroplastids are present.

Constituents.—Several alkaloids of marked toxicity (about 0.4 per cent), including: gelsemine (crystalline), sempervirine, gelsemidine and gelsemoidine; 6-methylesculetin or scopoletin (4-hydroxy-5-methoxy-coumarin); 0.5 per cent of a volatile oil; about 4 per cent of resins; several fatty acids; about 1.5 per cent of total ash and 0.25 per cent of acid-insoluble ash.

Gelsemine occurs in silky needles, and on the addition of nitric acid, yields a reddish solution which turns to dark green. Scopoletin is the aglycone of scopolin, a glucoside; both scopoletin and scopolin are found in scopola roots, belladonna root, scammonium root, etc. It may be obtained by microsublimation or by extraction with chloroform. A very dilute chloroformic solution of scopoletin slightly alkalinized with dilute ammonia causes a bluish green fluorescence in the ammoniacal layer.

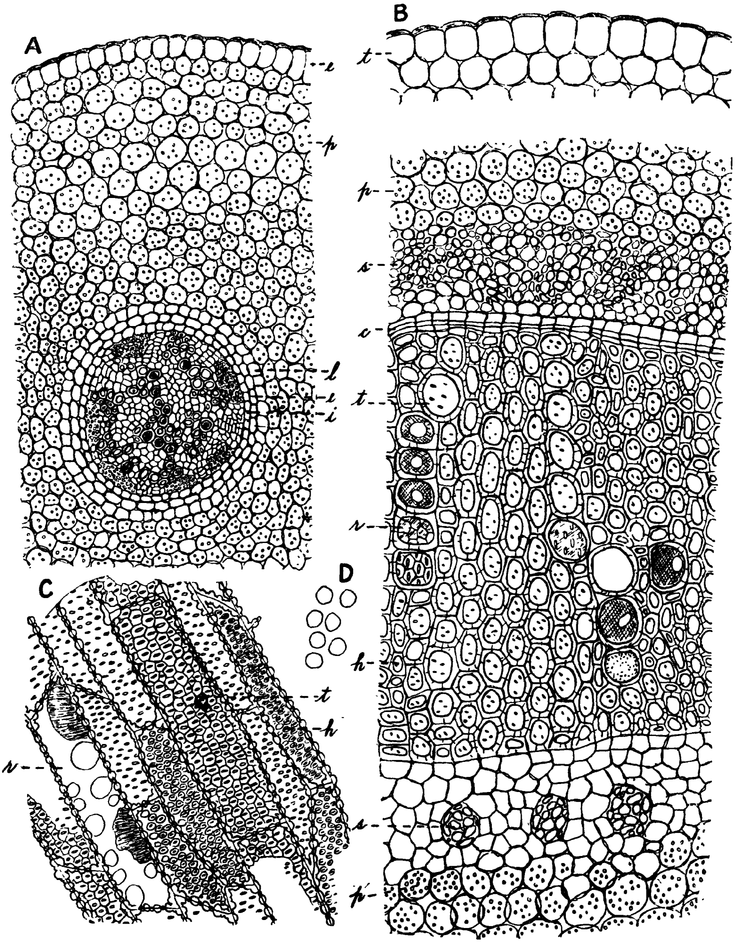


FIG. 276.—Pinkroot (*Spigelia marilandica*): *A*, transverse section of root showing epidermis (*e*); parenchyma containing starch (*p*); peripheral layer of central cylinder (*l*); the endodermis (*e*); a pericambial layer (*i*). The central cylinder consists of a 6- to 8-rayed fibrovascular bundle, and some of the tracheæ contain a brown gummy substance. *B*, Transverse section of rhizome showing epidermis (*t*), the outer wall of which contains a yellowish brown substance; parenchyma (*p*) of cortex containing starch; sieve (*s*); cambium (*c*); tracheæ (*t*); tracheæ (*r*) containing globular or somewhat irregular yellowish brown masses; tracheids (*h*); internal sieve groups (*s*); parenchyma of pith (*p'*) containing starch. *C*, Longitudinal section of the woody part of the rhizome. *D*, Isolated starch grains, which are from 2 to 5 microns in diameter.

Uses and Dose.—Gelsemium has a depressant action upon the central nervous system. It is an antispasmodic, a nervine, a sedative and a mydriatic. Average dose, 30 mg.

Spigelia or Pink Root (U. S. P. 1820 to 1926) is the dried rhizome and roots of *Spigelia marilandica* Linné, a perennial herb indigenous to the southern United States. Spigelia should be collected in autumn, carefully dried and preserved and kept no longer than two years. The rhizome is horizontal or oblique, more or less branched, 1.5 to 5 cm. in length, 2 to 5 mm. in diameter; externally dark brown, slightly annulate from scars of bud-scales, the upper portion with stem-scars and stem remnants, under and side portions with numerous roots and root-scars; the fracture is short; internally the bark is dark brown, with yellow, slightly radiate wood, and small pith; the odor is slightly aromatic and the taste bitter and pungent.

The roots are 5 to 10 cm. in length, about 0.3 mm. in diameter, with numerous rootlets; externally dark brown, longitudinally wrinkled; internally light brown, wood nearly cylindrical, porous. The structure is shown in Figure 276.

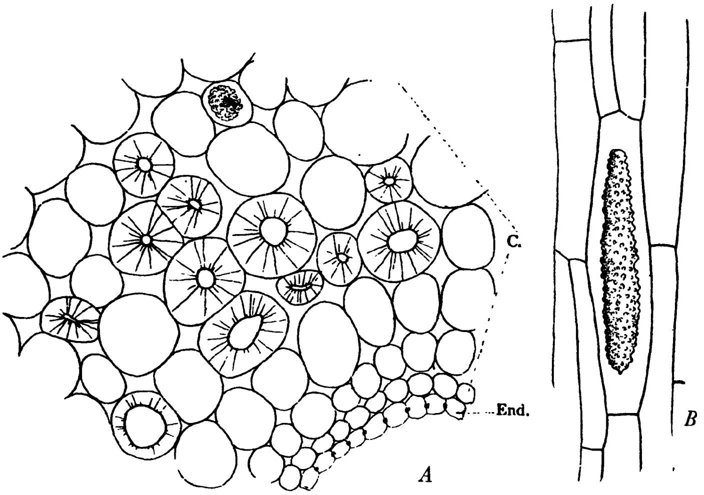


Fig. 277 —*Ruellia ciliosa*, the rhizome and roots of which are a common adulterant of Spigelia. *A*, Transverse section of a secondary root: *C*, cortical parenchyma with one cystolith and a number of stone cells with very thick walls and radiating simple pores: *End*, endodermis. *B*, Longitudinal section of the same root, showing a single cell with an elongated cystolith, the incrustation being of calcium carbonate. (After Holm.)

Powdered spigelia is grayish brown and shows spheroidal or slightly polygonal starch grains; conspicuous fragments containing lignified tracheæ and tracheids; fragments of tracheæ with spiral thickenings relatively few; bast fibers few, very long, non-lignified; occasional fragments of the reddish brown epidermal cells.

Spigelia contains a crystalline, volatile alkaloid, spigeline, which somewhat resembles coniine and nicotine and which forms precipitates with iodine or Mayer's reagent that are soluble in mineral acids; a bitter, acrid principle; volatile oil; resin; tannin; starch.

Spigelia is an anthelmintic.

While a very excellent and useful drug, spigelia has fallen into disrepute because of its extensive adulteration. For a number of years true spigelia has been substituted by or admixed with **Ruellia,** the rhizome and roots of Tennessee Pinkroot (*Ruellia ciliosa*, Fam. *Acanthaceæ*), and with Carolina Pink (*Phlox* *ovata*, Fam. *Polemoniaceæ*), both perennial herbs growing in woods and thickets of the southern United States.

Ruellia is easily distinguished from spigelia by large cystoliths in some of the cortical parenchyma cells, by strongly lignified, elongated stone cells having thick, porous and lamellated walls present in the cortex, and by a compact zone of porous tracheæ and wood fibers present in the xylem.

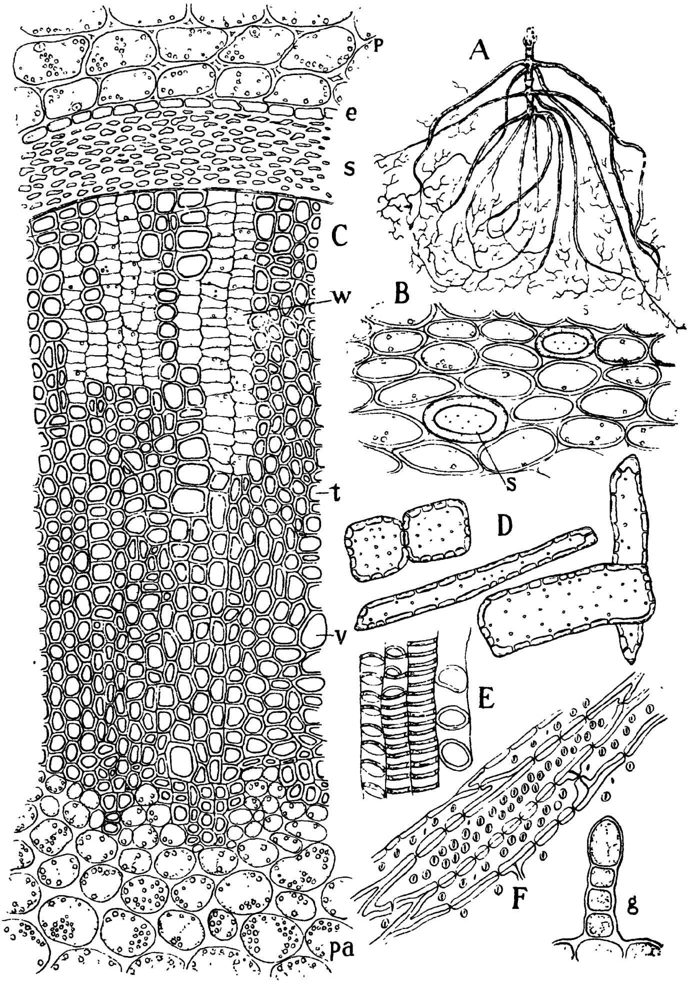


FIG. 278.—*Phlox ovata:* *A*, lower portion of plant showing long roots with numerous rootlets at the ends. *B*, Parenchyma from cortex of rhizome showing two sclerotic cells (*s*). *C*, Cross-section of portion of rhizome showing parenchyma of cortex (*p*) which contains protoplasm and starch grains, endodermis (*e*), phloem (*s*), tracheæ (*v*), wood fibers (*t*), wood parenchyma (*w*), parenchyma of pith containing starch grains and protoplasm (*pa*). *D*, Isolated sclerotic cells from cortex. *E*, Tracheæ having annular and spiral thickenings. *F*, Libriform cells. *G*, Glandular hair from the leaf.

The rhizome of Carolina Pink is very woody, the xylem occupying one-half of the radius of the section. The fibrovascular bundles are of the collateral type and there is a complete absence of intraxylary phloem, which is present in both spigelia and ruellia.

GENTIANACEÆ, OR GENTIAN FAMILY

This is a family of 70 genera and about 800 species of herbs, which are most abundant in temperate regions. The leaves are simple and usually opposite; the flowers are regular, and borne in terminal or axillary cymes; and the fruit is a capsule. Strands of interxylary phloem occur in several genera. The medullary rays are very narrow and sometimes entirely wanting. The non-glandular hairs are unicellular. Calcium oxalate crystals are wanting. Bitter principles are invariably present.

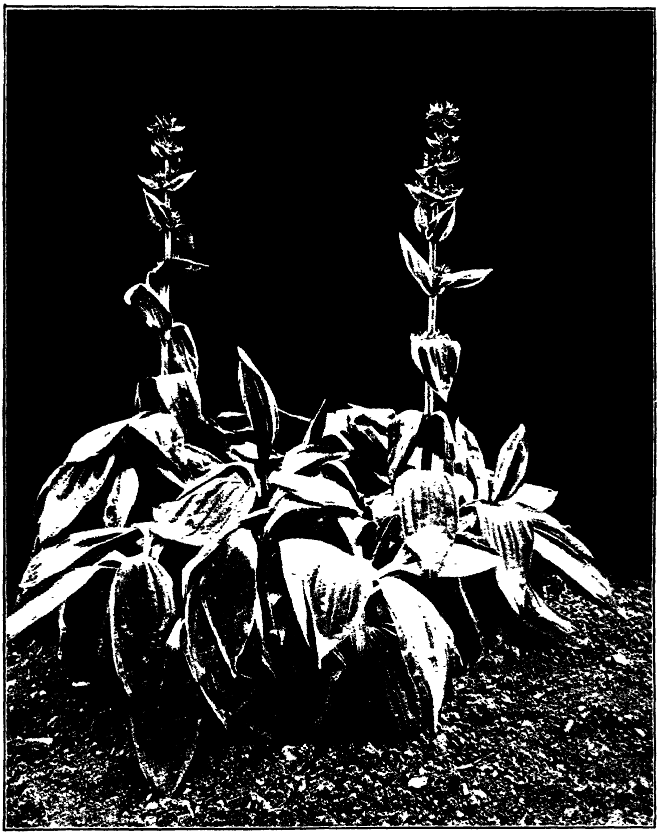


FIG. 279.—*Gentiana lutea*, growing in the Royal Botanic Society's Gardens (London) (After Pérrédès.)

GENTIAN

Gentian or Gentian Root (U. S. P. 1820 to date) is the dried rhizome and roots of *Gentiana lutea* Linné. Gentian yields not less than 30 per cent of water-soluble extractive and contains not more than 15 per cent of moisture. *Gentiana* was named after Gentius, king of Illyria, discoverer of the tonic value of the plant; *lutea*, yellow, refers to the color of the flowers. The plant is a large perennial herb indigenous to central and southern Europe and Asia Minor. The drug is gathered in the autumn and is cut into pieces of variable length, the more fleshy ones being sliced longitudinally. These are then left in piles and allowed to ferment, after which they are slowly dried. Prepared in this way the internal color of the root changes from white to yellowish brown and a considerable amount of the gentiopicrin disappears, probably through enzymic action. The drug is packed in burlap bags, most of the commercial supply coming from Marseilles, Bordeaux, Antwerp, Hamburg and Budapest.

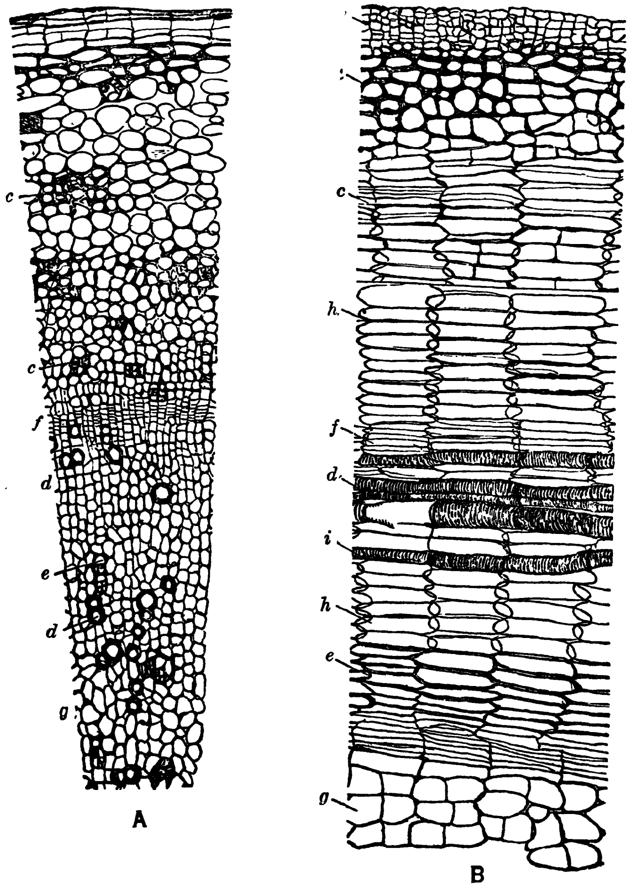


FIG. 280.—*A*, Transverse and (*B*) longitudinal sections of Gentian: *a*, cork of 4 to 6 rows of thin-walled cells; *b*, hypodermal-like outer cortex; *c*, phloem region of thin-walled parenchyma and small strands of sieve; *f*, the distinct cambium layer; *e*, elongated but unlignified fiber-like cells (intermediate fibers); *h*, somewhat elongated parenchyma cells; *g*, short, brown, thin-walled parenchyma forming most of the xylem region; tracheæ small scattered; medullary rays indistinct. (After Meyer.)

Gentian was known to Pliny and Dioscorides. It was commonly used in medicine during the Middle Ages.

Description.—Nearly cylindrical to irregular pieces, 5 to 40 mm. in diameter; externally light brown, annulate above (rhizome portion), longitudinally wrinkled below (root portion), and with a few buds, stem- and root-scars; fracture short when dry, tough and flexible when damp; internally yellowish brown, with a distinct dark brown cambium zone.

Structure.—See Figure 280.

Powder.—Moderate yellowish brown; odor strong and characteristic; taste persistently and strongly bitter; fragments of parenchyma tissue with occasional tracheæ having simple pores; intermediate fibers non-lignified, the walls being marked with irregular, simple, oblique pores; starch grains or calcium oxalate crystals few or absent; stone cells and bast or wood fibers absent.

Constituents.—Three bitter glucosides, gentiopicrin, gentiamarin and gentiin; gentisin; gentianose; glucose 12 to 15 per cent; total ash about 3 per cent; acid-insoluble ash about 0.75 per cent. Gentiopicrin forms white, optically levorotatory needles, soluble in water, less so in alcohol, and may be largely destroyed by enzymes during curing and drying of the drug. Gentiamarin is amorphous, with a bitter taste. Gentiin (gentianin) occurs in microscopic yellow needles, gives a greenish black color with solutions of ferric salts and on hydrolysis yields gentienin, xylose and glucose. Gentianose is a crystalline carbohydrate, occurring in the fresh root, and does not reduce Fehling's solution. Gentisin or gentianic acid may be microsublimed from powdered gentian to form yellow prismatic crystals, from 10 to 150 microns long, straight or slightly curved, and isolated or in small clusters; they are insoluble in water (hence tasteless), alcohol or ether, but soluble in chloral hydrate or potassium hydroxide solutions.

Uses and Dose.—Gentian is a bitter tonic. Average dose, 1 gm.

Gentiana Catesbæi, Blue Gentian or American Gentian (U. S. P. 1820 to 1882) is the rhizome and roots of *Gentiana Catesbæi* Elliott, now embracing the three common blue gentians in eastern United States, namely: *G. puberula* Michaux, *G. Saponaria* Linné (*G. Catesbæi* Walter), and *G. Andrewsii* Grisebach. The rhizome and roots are small, much wrinkled on drying, light brown externally, with the distinctive odor and persistent bitter taste of Gentian. It is used in the same dosage and for the same purposes as the European drug.

Allied Plants.—The rhizomes and roots of various other European species of *Gentiana* are sometimes collected and employed medicinally, as of *Gentiana purpurea*, collected in Switzerland, and *G. pannonica* and *G. punctata*, collected in Austria.

Chirata (U. S. P. 1863 to 1916; N. F. 1916 to 1936) is the dried plant of *Swertia Chirayita*, an annual herb indigenous to the mountains of northern India. The generic name *Swertia* was applied in honor of Emanuel Swert, an herbalist of the seventeenth century. The plants are collected after the capsules are fully formed.

The drug occurs in flat bundles tied with strips of bamboo and about 1 meter in length. Root simple, tapering, about 7 mm. in thickness near the crown. Stem about 1 meter in length, cylindrical, flattened quadrangular above, each angle with a decurrent wing, yellowish or purplish brown and with many ascending branches; wood yellowish; pith lemon-yellow, easily separable from the wood, sometimes wanting. Leaves opposite, sessile, ovate-lanceolate, about 6 cm. in length, entire, midrib prominent and with 3 to 7 parallel lateral veins. Inflorescence a large panicle; flowers numerous, regular; calyx and corolla each 4-lobed. Capsule ovoid, acute, unilocular, many-seeded.

The powder is dark yellow, odor slight, taste extremely bitter; it contains tracheæ with spiral, scalariform or simple pore markings; sclerenchyma fibers more or less lignified; pollen grains oblong or ellipsoidal, very prickly, about 20 microns in diameter; collenchyma cells with yellowish brown resin and tannin masses.

Chirata contains a bitter glucoside chiratin, which is precipitated by tannin and yields on hydrolysis two bitter principles; ophelic acid and chiratogenin, the latter being insoluble in water. Ophelic acid is a brown hydroscopic substance which is readily soluble in water and in alcohol. The drug also contains resin, tannin and 4 to 8 per cent of ash.

Chirata is a bitter tonic. Other species of *Swertia*, as well as other bitter plants known in India as "chiratta," find their way into the market, but are easily distinguished from the true drug.

Centaury or Centaurea Minor (N. F. 1916 to 1936) is the dried flowering plant of *Erythræa Centaurium* (Linné) Persoon. The plant is an annual herb indigenous to Europe, but naturalized in southeastern Canada and northeastern United States. The herb, without the roots, is gathered at the time of flowering in July, dried and tied into small bundles. It has been highly prized in European medicine for many centuries. The name is from the Latin *centum* and *aurum* meaning "hundred gold pieces" in allusion to its alleged priceless value.

The drug is glabrous, the stem from 15 to 50 cm. long, much branched from the base, but little branched, if at all, from above; slender, sharply angled or narrowly winged, sparsely leafy; leaves opposite, entire, mostly 3-nerved, sessile, those at the base obovate and obtuse, from 2 to 5 cm. in length, their base narrowed and petiole-like, those of above gradually changing to oval, then ovate or even lance-linear, acute; flowers in a terminal compound cyme, rose-colored; calyx from 5 to 7 mm. in length, deeply 5-parted, the tube short, sharply angled, lobes linear-attenuate with a sharp midrib; corolla tube nearly twice the length of the calyx, slender; the limb from 10 to 15 mm. in breadth, its lobes broadly oblong or oval; stamens five, exserted, bright-yellow, their anthers twisted when old; pistil two-carpled. Odor faint but characteristic; taste persistently bitter.

Centaury yields not more than 5 per cent of ash.

Centaury contains a bitter principle; a volatile oil; a resin; erytaurin, a colorless crystalline glucoside; erythrocentaurin, a crystalline tasteless principle, which is colored red on exposure to the light. Also mucilage and wax.

Centaury is a tonic and a febrifuge.

Sabbatia or American Centaury (U. S. P. 1820 to 1882) is the overground plant of *Sabbatia angularis*, a biennial herb growing in rich soil and moist meadows throughout the eastern United States and Canada. The drug should be collected at the time of flowering, but the commercial drug frequently is devoid of leaves and flowers and consists of the stems with their capsular fruits.

The stems are very light green, yellowish or pinkish, glabrous, distinctly 4-angled above, each angle with a thin, membranous wing-like ridge of collenchyma; fracture fibrous; pith hollow. The leaves are ovate or oblong, cordate and clasping at base; acute apex, entire margin, thin, olive-green, palmately veined. The flowers are in cymes, rose-pink, with 5-parted calyx and corolla, the latter rotate, the segments obovate-elliptical, about 1.5 cm. long; stamens 5; ovary and style 1. Fruit is a 2-valved, oblong or ovoid capsule, dark brown and covered with resin. Seeds are numerous, deeply reticulate and very small.

Sabbatia contains a bitter principle, 3.75 per cent; erythrocentaurin; a volatile oil; a greenish resin; mucilage; sugars; ash 2.85 per cent. It is used as a tonic.

Menyanthes, Buckbean or Marsh Trefoil (U. S. P. 1820 to 1842; N. F. 1916 to 1926) is the dried leaf of *Menyanthes trifoliata*; a low perennial herb, having thick, horizontal rhizomes and growing in bogs in the northern United States and from Greenland to Alaska.

The plant is indigenous to Europe and Asia, and the leaves are official in several foreign pharmacopœias. The drug is gathered in May or June, at the time of flowering. The leaves are 3-foliate, having sheathing petioles 7 to 15 cm. in length; leaflets are nearly sessile, elliptical or ovate, up to 8 cm. in length and 4 cm. in breadth, apex obtuse or rounded, base spatulate, margin entire, occasionally somewhat undulate, and bearing hydrathodes, olive-green and glabrous; odor distinct, slight; taste very bitter. In the petiole and mesophyll are large intercellular air spaces with large, branching, thick-walled, lignified cells, the branches curving around the interior of the spaces, thus strengthening the leaf structure and maintaining the open air-channels. When the leaf is dried these spaces tend to shrink and collapse.

Menyanthes contains a bitter glucoside, menyanthin, yielding on hydrolysis glucose and menyanthol; a mixture of fatty acids, occurring in the form of esters of cholestrin and ceryl alcohol; a reddish yellow coloring principle, resembling carotin; also cane sugar and chlorophyll. Natural ash about 8.5 per cent, with 0.35 per cent insoluble in diluted hydrochloric acid.

Menyanthes is a tonic and a febrifuge.

APOCYNACEÆ, OR DOGBANE FAMILY

This is a large family, comprising 155 genera and over 1000 species of perennial herbs, shrubs and trees. They are very widely distributed, occurring mostly, however, in tropical regions. The leaves are usually opposite, the flowers regular and 5-merous, and the fruits are either follicles or drupes. Non-articulated laticiferous tubes are present in all parts of the plants of this family, developed very early, being present even in the embryo. They usually have thin walls and narrow lumina, and the contents may be a caoutchouc-like substance, so that on the fracture of the bark it may be drawn out into thin threads as in the *Celastraceæ*. The latex may also contain starch grains and distinct nuclei. Secretory cells are also present in the barks of some of the genera, as *Aspidosperma*. Strands of intraxylary phloem occur in the pith. Calcium oxalate is secreted in the form of solitary crystals, styloids or rosettes. The non-glandular hairs are either unicellular or uniseriate. Glandular hairs are wanting, except in the leaves of the oleander, in which the hairs consist of several rows of elongated cells, which are covered with a palisade-like secretory epidermis. In the oleander the stomata are situated in deep pits, which are covered with long hairs.

APOCYNUM

Apocynum, Black Indian Hemp, Dog's Bane or Canada-hemp (U. S. P. 1820 to 1916; N. F. 1916 to date) consists of the dried rhizome and roots of *Apocynum cannabium* Linné (U. S. P. 1831 to 1916; N. F. 1916 to date) or of *Apocynum androsæmifolium* Linné (U. S. P. 1820 to 1882; N. F. 1942 to date). Apocynum possesses a potency such that 0.1 gm. of it is equivalent to not less than 2 U. S. P. XIII Digitalis Units.

Apocynum is from the Greek meaning dog's bane; *cannabium* is the Greek name for hemp. The plants are perennial herbs growing in fields and thickets in the United States and southern Canada. The fibrous bark was long used by the Indians for domestic purposes. Since the days of the earliest settlers, who learned its properties from the Indians, the root of *Apocynum* has been used as a diuretic and a remedy in dropsy.

Description.—Cylindrical, somewhat branched, usually broken into pieces, 3 to 15 mm. in diameter; externally light brown, longitudinally wrinkled and transversely fissured, with a few rootlets or rootlet scars; fracture short; internally, bark light brown, up to 3 mm. in thickness, easily separable from the lemon-yellow, porous, slightly radiate wood.

Stem fragments are distinguished by having a comparatively thin, finely fibrous bark and a hollow center.

Structure.—See Figure 281.

Powder.—Light yellowish brown; odor saponaceous; taste starchy, bitter, somewhat acrid; starch grains numerous, up to 20 microns in diameter, spheroidal, ellipsoidal, ovoid, pyriform or irregular, with a hyaline central cleft and distinct polarization crosses; numerous, slender, lignified, porous wood fibers associated with tracheæ having simple pits or elliptical bordered pores; stone cells from *A. androsæmifolium* isodiametric or elongated, with strongly lignified thick walls and branching pore canals; few fragments of cork with brown to yellow cell walls; fragments of parenchyma associated with latex cells.

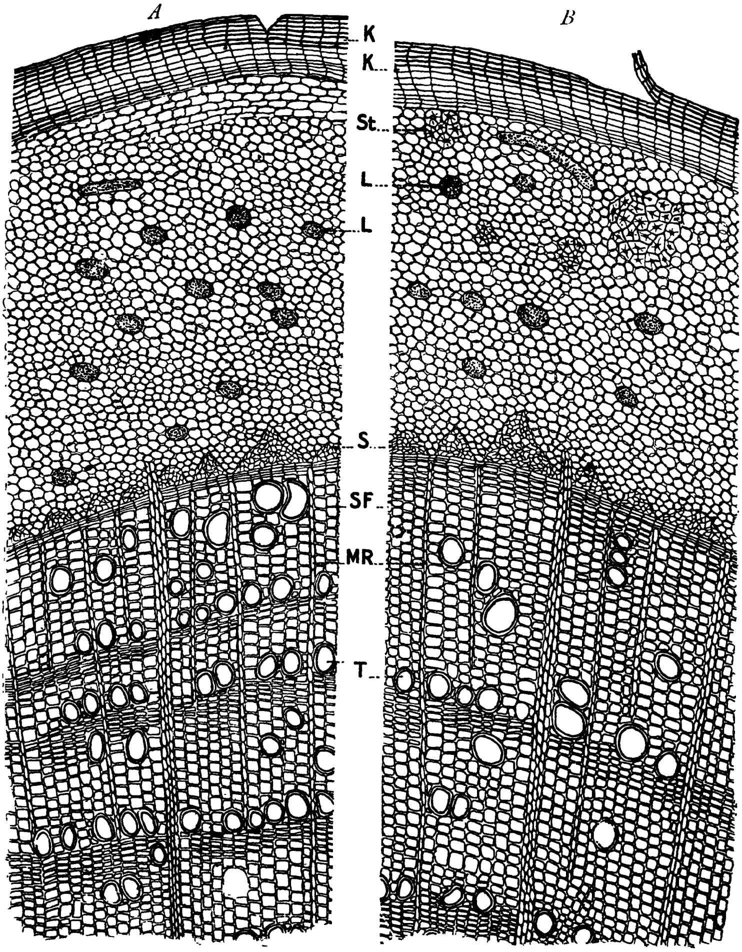


Fig. 281.—*A*, Transverse section of the root of *Apocynum cannabinum* showing cork (*K*); laticiferous tubes (*L*) in the cortex; sieve (*S*), beneath which is the cambium zone; wood fibers (*SF*), tracheæ (*T*), and medullary rays (*MR*). *B*, Transverse section of the root of *Apocynum androsœmifolium* showing in addition groups of stone cells (*St*) in the cortex.

Constituents.—Cymarin (apocynamarin), a dilactone of Kiliani's oxydigitogenic acid, or of an isomeride, forms small rhombic pyramids which are sparingly soluble in water but freely soluble in alcohol, chloroform and acetone; it is extremely bitter and represents the cardiac activity of the drug. Apocynin

(0.2 per cent) occurs in slender colorless prisms with a slight odor of vanillin and apparently is identical with acetovanillin; it is almost inactive pharmacologically. There are also present a glucoside, apocynein, with cardiac action; a volatile oil; resin, tannin; and starch; about 3 per cent of total ash and 0.3 per cent of acid-insoluble ash.

Uses and Dose.—Apocynum belongs to the digitalis series of drugs. It is a diuretic, an expectorant, a cardiac stimulant, a diaphoretic and an emetic. Average dose, 0.2 gm.

Pharmacologically, *A. androsæmifolium* root is not equivalent to *A. cannabinum* root; the latter gives a much stronger cardiac stimulation, while the former has been used as a diuretic and cathartic.

The tolerance of the patient to the possible toxic or cumulative action of the drug should be carefully observed and the dosage regulated accordingly.

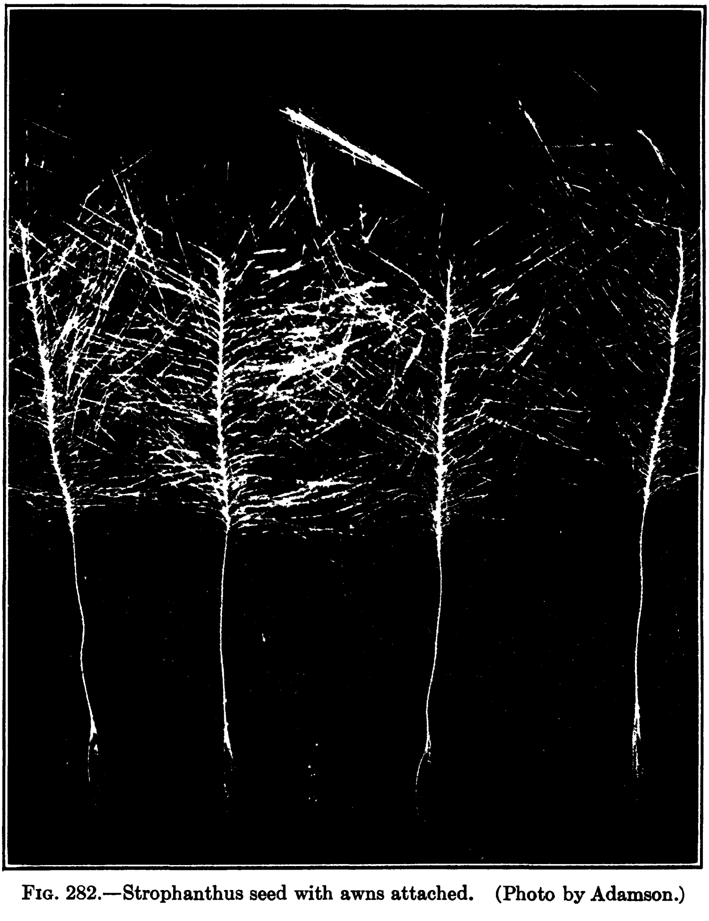


Fig. 282.—Strophanthus seed with awns attached. (Photo by Adamson.)

STROPHANTHUS

Strophanthus (U. S. P. 1894 to 1936; N. F. 1936 to date) is the dried, ripe seed of *Strophanthus Kombe* Oliver, or of *Strophanthus hispidus*

DeCandolle, deprived of the awns, and possesses a potency, per gram, equivalent to not less than 55 mg. of U. S. P. Reference Ouabain, when assayed by the prescribed method as given in the monograph on Strophanthus Tincture in the National Formulary.

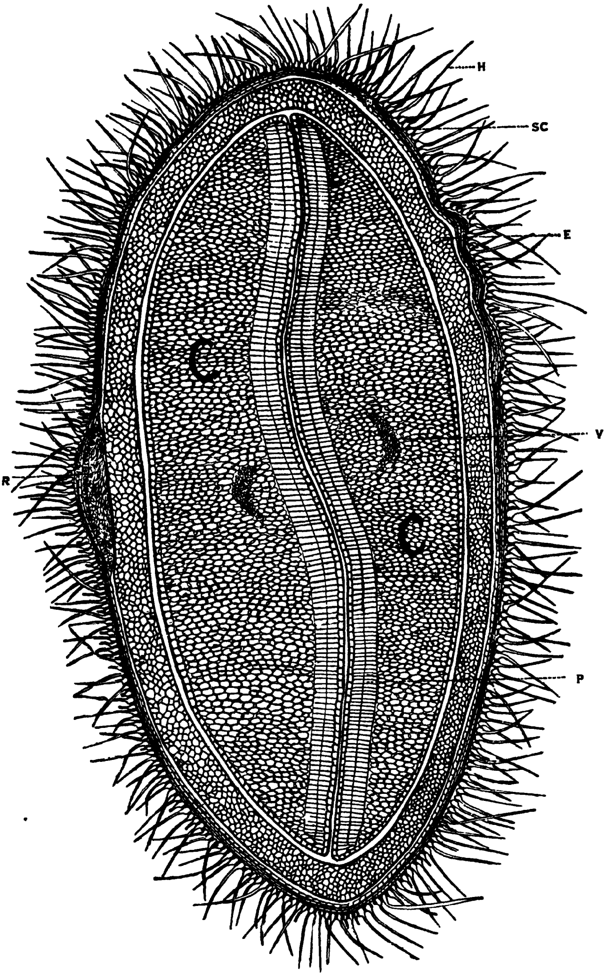


FIG. 283.—Transverse section of strophanthus seed: *SC*, seed coat, with numerous, unicellular hairs (*H*) usually bent, and arising in *S. kombe* seed from the center of the surface of the epidermal cell and in *S. hispidus* seed from near the radial wall; *R*, raphé tissue; *E*, endosperm of 5 to 30 rows of cells containing aleurone, fixed oil and strophanthin; *C*, *C*, the two long plano-convex cotyledons of thin-walled parenchyma bearing aleurone and fixed oil; *V*, fibrovascular bundle in cotyledon; *P*, palisade cells of cotyledon; the short straight caulicle and small radicle do not appear in the drawing.

Strophanthus is from the Greek meaning "a turn or twist," and "a flower," and refers to the twisted lobes of the corolla; *hispidus* means hairy, referring to the hairy character of the plant; *Kombi* is the native

African name for the seed. The 30 species of *Strophanthus* native to Africa are perennial woody climbers which frequently hang from the trees in festoons. The fruits are gathered when ripe, the mesocarp stripped off and the seeds dried in the endocarp. The awns of the seeds (see Fig. 282), are removed before packing and shipping. The seeds of green Strophanthus (*S. Kombe*) are largely collected in East Africa near Lakes Tanganyika and Nyassa. Brown Strophanthus seeds (*S. hispidus*) come largely from Senegambia and Guinea in western Africa. Strophanthus seeds have long been used by the native Africans in the preparation of arrow poisons. These were first observed by Hendelot in western Africa and by Livingstone in East Africa. Early specimens sent to Europe established the powerful cardiac properties of the seeds. Strophanthin was isolated in 1865, soon after which the drug was adopted by the medical profession.

DESCRIPTION.—*Strophanthus Kombe* seed: oblong-lanceolate or spatulate, unevenly flattened and in transverse section deltoid, 8 to 25 mm. in length, 2.5 to 5 mm. in breadth, 1 to 2 mm. in thickness; externally pale yellow with a greenish tinge, covered with long hairs giving a silky appearance to the seed, the raphé extending as a distinct ridge from the hilum about half the length of the seed; internally, grayish, endosperm about 0.2 mm. in thickness, cotyledons plano-convex; inodorous except when broken; taste very bitter.

Strophanthus hispidus seed: externally light to dark brown and without the greenish tinge; somewhat smaller and less hairy.

STRUCTURE AND POWDER.—See Figures 283, 284 and the National Formulary.

CONSTITUENTS.—Strophanthin or *K*-strophanthin, a mixture of glycosides, up to 5 per cent; about 30 per cent of fixed oil; kombic acid; trigonelline and choline; natural ash, about 4 per cent and acid-insoluble ash, about 0.25 per cent. *K*-strophanthin may contain the glycosides *K*-strophanthin-*b* and cymarin. *K*-strophanthin-*b* hydrolyzes into cymarin and glucose, and cymarin hydrolyzes into strophanthidin and cymarose. Strophanthidin is the aglycone of several cardiac-stimulant glycosides, such as strophanthin, scillarin, digitoxin and cymarin.

STANDARDS AND TESTS.—The endosperm tissue either in the cut seed or in powder form, usually assumes a dark green color when brought into contact with sulfuric acid.

Prismatic crystals of calcium oxalate should be absent in the seed coat (distinction from *Strophanthus courmontii*).

USES AND DOSE.—Strophanthus belongs to the digitalis series of drugs and has an action very similar to digitalis. It is a heart tonic and a diuretic. Average dose, 0.06 gm.

ADULTERANTS AND ALLIED PRODUCTS.—The seed of other species of *Strophanthus*, growing in the same regions with *S. kombe*, sometimes occur in commerce. For *Strophanthus gratus* see Ouabain, page 510.

The seed of *S. sarmentosus*, a small tree growing in Africa, from Senegal to Congo Free State, are shorter, thicker and more sparingly hairy than those of *S. kombe*.

The seed of *Kickxia africana*, a tree growing in western tropical Africa, are spindle-shaped, not flattened, slightly twisted, not hairy and of a reddish brown color. The cotyledons are somewhat folded and not parallel as in *Strophanthus kombe*. With sulfuric acid the seeds are colored brown, changing to red.

The seed of *Strophanthus courmontii* resemble those of *S. kombe* but contain calcium oxalate and give a red color on treatment with sulfuric acid.

Strophanthin (U. S. P. 1905 to 1947; N. F. 1947 to date) is a glycoside or a mixture of glycosides obtained from *Strophanthus Kombe* Oliver.

Strophanthin, when assayed as directed in the National Formulary monograph, shall possess a potency per mg. equivalent to 0.5 mg. U. S. P. Ouabain Reference Standard. Strophanthus seeds are defatted with petroleum benzin, after which they are extracted with dilute alcohol. Impurities are removed from the alcoholic solution, after which it is concentrated, *in vacuo* and the strophanthin precipitated. It occurs as a white or yellowish white powder. Consult the National Formulary for its constants and properties.

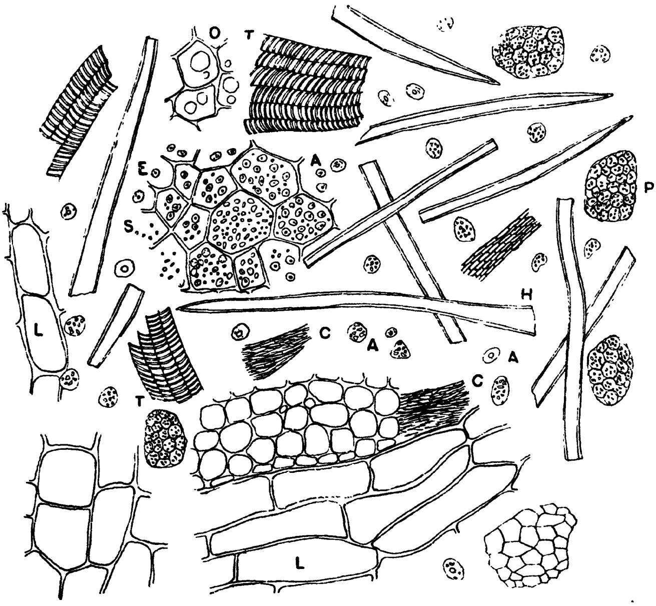


FIG. 284.—Strophanthus, Powdered: *L*, surface view of epidermal cells with thickened, lignified walls and bases of hairs; *H*, hairs, mostly in fragments, but up to 800 microns long when entire, and with rather thin, somewhat lignified walls; *P*, parenchyma of endosperm and cotyledons containing aleurone (*A*) up to 8 microns in diameter, a fixed oil (*O*) and minute starch grains (*S*); *T*, tracheal fragments; *C*, collapsed cells of seed coat.

USES AND DOSE.—Strophanthin is a cardiac tonic and a diuretic. Average dose 0.5 mg. It is extremely poisonous.

Ouabain or G-Strophanthin (U. S. P. 1942 to date; as Reference Standard U. S. P. 1916 to date) is a glycoside ($C_{29}H_{44}O_{12}.8H_2O$) obtained from the seed of *Strophanthus gratus* (Wall. et Hook.) Baillon. The potency of ouabain, assayed biologically, corresponds to the potency of 91 per cent of an equal weight of U. S. P. Ouabain Reference Standard.

The seeds are spindle-shaped, somewhat flattened, of a light yellow or orange brown color, nearly free from hairs and have a peculiar bitter taste. With 90 per cent sulfuric acid, the cells of the endosperm are colored reddish, becoming violet. Ouabain is prepared by much the same process as strophanthin.

Ouabain occurs as white, odorless crystals or as a crystalline powder. It is extremely poisonous. It is fairly soluble in water and in alcohol. For Constants and Tests of Identity see the U. S. Pharmacopœia.

Ouabain has been used for years as a reference standard in the assay of cardiac-stimulant drugs, largely because it is a pure definite chemical, but also because its cardiac-stimulant action is rapid. Therapeutically, it is used intravenously for very prompt effect. Average dose, 0.25 mg.

Aspidosperma, Quebracho or Quebracho Blanco (U. S. P. 1894 to 1905, 1916 to 1926) is the dried bark of *Aspidosperma quebracho blanco*, a large tree indigenous to the western provinces of the Argentine Republic, Chile, Bolivia and Southern Brazil.

Aspidosperma occurs in irregular chips or in longitudinal pieces; bark from 1 to 3.5 cm. in thickness; periderm very thick, deeply furrowed, frequently with deep fissures; inner surface occasionally with adhering wood, otherwise light yellowish to light reddish brown, finely longitudinally striate and porous; fracture short-fibrous with projecting bast fibers; nearly inodorous; taste bitter and slightly aromatic.

The periderm consists of strands of reddish yellow cork, separated by large groups of stone cells, isolated bast fibers and parenchyma; inner bark has starch-bearing medullary rays from 1 to 5 cells in width separating narrow wedges composed of parenchyma, large groups of stone cells and an occasional bast fiber, the latter very thick-walled, strongly lignified and surrounded with crystal fibers.

The powder is reddish brown; and contains calcium oxalate prisms frequently terminated by pyramids, and up to 30 microns in length; stone cells numerous, more or less tabular; cork cells somewhat polygonal and with thick, slightly lignified walls; starch grains, from 3 to 25 microns in diameter, single or 2- and 4-compound, the individual grains spheroidal, ovoid or more or less plano-convex.

The bark contains a mixture of alkaloids, about 1.5 per cent, the most important of which are aspidospermine and quebrachine. Aspidospermine is colored brownish with sulfuric acid and potassium dichromate, changing to cherry-red or purplish. Quebrachine is colored yellow with perchloric acid. The other alkaloids are named aspidosamine, aspidospermatine, quebrachamine, hypoquebrachine.

The drug contains 3.5 per cent of tannic acid; a cholesterin-like body, quebrachol; a sugar, quebrachit; and total ash, of a white or greenish white color, about 6.4 per cent, with about 0.4 per cent of acid-insoluble ash.

Aspidosperma is a heart and respiratory stimulant. It is also a diuretic and an antipyretic.

Quebracho Bark, the bark of *Aspidosperma quebracho colorado*, contains 20 per cent of tannic acid. A commercial extract is made from the bark, which is used in the tanning of leather.

ASCLEPIADACEÆ, OR MILKWEED FAMILY

This is a large family of perennial herbs, comprising about 1700 species. They are most abundant in North America. The leaves are opposite or whorled; the flowers usually have a 5-parted corona between the corolla and stamens, which is adnate to one or the other; the fruits are follicles. The anatomical characters resemble very closely those of the *Apocynaceæ*. In the pericycle occur either solitary or small groups of bast fibers. The latter are not found in the secondary cortex. Both the glandular and non-glandular hairs are either unicellular or uniseriate.

Condurango (N. F. 1916 to 1947) is the dried bark of *Marsdenia cundurango* Richenbach filius. *Marsdenia* was named in honor of William Marsden (1784–1836), who wrote a history of Sumatra; *condurango* is said to mean "the condor-vine," and comes from the Spanish. The plant is a somewhat prostrate or climbing shrub, indigenous to the lofty mountains of Ecuador and Peru. Condurango has long been used as a remedy by the natives of western South America. It was introduced into European and North American medicine about 1871. The drug seems to have won greater favor in Europe where it is official in several Pharmacopœias.

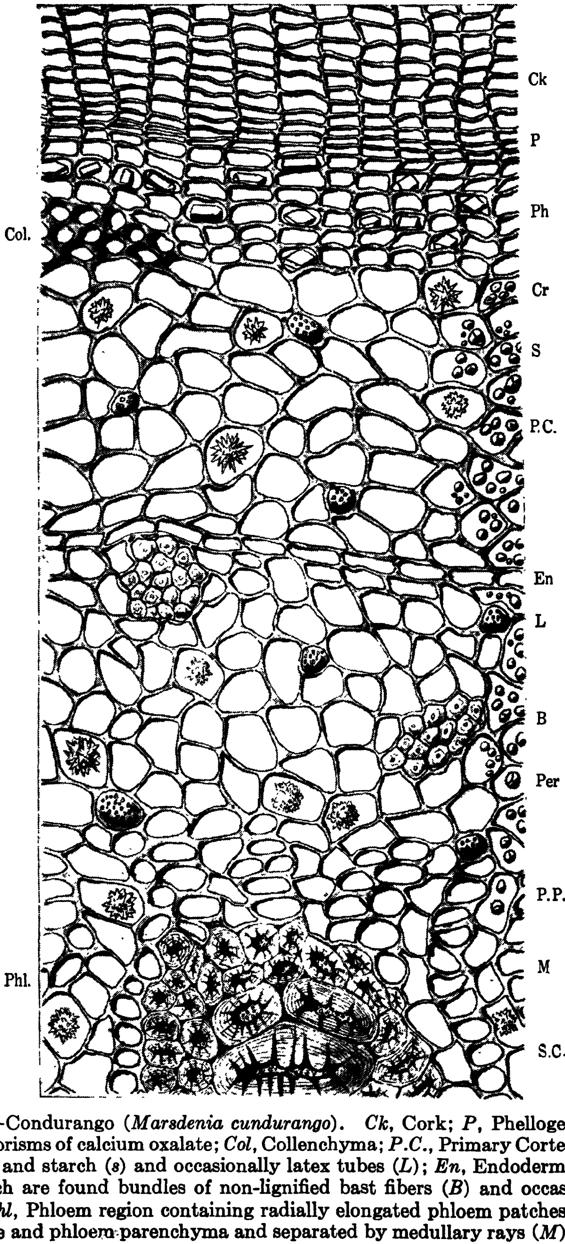


FIG. 285.—Condurango (*Marsdenia cundurango*). *Ck*, Cork; *P*, Phellogen; *Ph*, Phelloderm with prisms of calcium oxalate; *Col*, Collenchyma; *P.C.*, Primary Cortex, containing rosettes (*cr.*) and starch (*s*) and occasionally latex tubes (*L*); *En*, Endodermis; *Per*, Pericycle in which are found bundles of non-lignified bast fibers (*B*) and occasionally latex tubes (*L*); *Phl*, Phloem region containing radially elongated phloem patches (*P.P.*) composed of sieve and phloem parenchyma and separated by medullary rays (*M*) 2 cells wide; *S.C.*, stone cells. (Drawing by E. H. Wirth.)

In single quills or transversely curved pieces, bark from 1 to 6 mm. in thickness; outer surface pale brown to dark brown, nearly smooth, and with numerous lenticels, or having a more or less soft-scaly and considerably roughened cork, occasionally with brownish black apothecia of a lichen; inner surface grayish white or light brown, longitudinally striate; fracture short and granular or short fibrous.

For the structure, see Figure 285.

The powder is light yellowish brown with a slight aromatic odor, especially marked in the fresh drug, and a bitter, aromatic taste. The stone cells are more or less irregular in shape, with very thick, porous walls; calcium oxalate occurs chiefly in rosettes, occasionally in single prisms, mostly 10 to 35 microns in length; starch grains are up to 20 microns in diameter, single or 2- to 4-compound; bast fibers are non-lignified, very long and from 10 to 35 microns in width; fragments of thin-walled latex cells from 15 to 30 microns in diameter and filled with a granular substance.

Condurango contains condurangin, a yellow, amorphous, hydroscopic, bitter powder, probably a combination of glycosides. It is not completely soluble in water and is precipitated as a cloud upon heating the aqueous solution. There is also present tannin, 12 per cent; 0.75 per cent of a deliquescent crystallizable acid; a yellowish white resin; a small quantity of starch; a fixed oil; a fermentable sugar; and about 8.3 per cent of total ash with about 0.3 per cent of acid-insoluble ash.

Condurango is a stomachic bitter, an astringent and an alterative. It is especially useful for diseases of the gastric mucosa. Average dose, 4 gm.

Asclepias, Asclepias Tuberosa, Pleurisy Root or Butterfly Weed (U. S. P. 1820 to 1905; N. F. 1916 to 1936):

Asclepias Incarnata, Flesh-colored Asclepias or Swamp Milkweed (U. S. P. 1820 to 1863, 1873 to 1882):

Asclepias Seriaca or Common Milkweed (U. S. P. 1820 to 1863, 1873 to 1882) are the dried roots, respectively, of *Asclepias tuberosa* Linné, *A. incarnata* Linné, and of *A. syriaca* Linné.

These plants are indigenous to the eastern United States and southern Canada (except *A. tuberosa* is not found in Canada) and extending southward and westward. They are large perennial herbs with flowers in axillary or terminal umbels. The follicular fruit are rather large, and the seed have tufts of long silky hairs. *A. tuberosa* prefers sandy soils and produces beautiful orange-colored flowers; *A. incarnata* prefers wet ground and *A. syriaca* rich dry soils.

The drugs are collected in the fall and the thicker pieces sliced to facilitate drying. The rhizomes are horizontal or upright and up to 25 mm. thick; the roots are usually long and those from *A. tuberosa* are up to 5 cm. in thickness. Externally from gray brown to orange brown, furrowed, with stem remnants and stem scars on the rhizomes, and rootlet scars on the roots. Fracture short, tough; bark thin, wood yellow, medullary rays white and finely radiate; pith wanting, except in the rhizome, where it is whitish, with numerous yellow stone cells.

The powder is light brown, the odor slight and the taste starchy, bitter and acrid; calcium oxalate rosettes occur from 15 to 50 microns in diameter; starch grains are 3 to 15 microns in diameter, single and 2- to many-compound, the individual grains spheroidal, plano-convex or irregularly polyhedral, having a large central circular marking or transverse fissure: large groups of orange-yellow stone cells; a few wide tracheæ, having either simple pores or scalariform perforations, and associated with short wood fibers having thin porous walls.

The drug contains a yellowish glucoside, asclepiadin, having the taste of the drug and apparently the active principle. It is soluble in hot water and alcohol, colored green with sulfuric acid and pink with nitric acid, changing to purple. Asclepias also contains a volatile oil; several resins; tannic acid; starch; pectin; gum; a fixed oil; and calcium oxalate.

Asclepias is a diaphoretic and expectorant. In large doses it is an emetic and a purgative.

CONVOLVULACEÆ, OR MORNING GLORY FAMILY

This is a family of about 1100 species, very abundant in the tropics. They are either herbs or shrubs, some being more or less trailing and frequently climbing. The leaves are alternate, the flowers have gamopetalous corollas and the fruits are capsules. Secretory cells, having suberized walls, occur either as isolated cells or arranged in long vertical rows, and contain a colorless or yellowish brown milky substance, which is soluble in alcohol. Latex vessels are rarely found.

The fibrovascular bundles with few exceptions are of the bicollateral type. Calcium oxalate is secreted in the form of small needles, small rods, solitary crystals and rosettes, the rosettes sometimes occurring in the idioblasts of the leaves. The non-glandular hairs usually consist of 2 cells, the stalk cell having a suberized wall. The glandular hairs usually have a unicellular stalk and a multicellular head. In the leaves, the neighbor cells are placed parallel to the pores of the stomata. A very complicated anomalous structure is seen in the fleshy roots of jalap and scammony.

JALAP

Jalap or Jalap Root (U. S. P. 1820 to 1936; N. F. 1936 to date) is the dried tuberous root of *Exogonium purga* (Wendoroth) Bentham. Jalap yields not less than 9 per cent of resin which meets the tests of Jalap Resin, page 515, and not more than 0.5 per cent of acid-insoluble ash. *Exogonium* is from the Greek meaning "outside" and "offspring," in allusion to the exserted stamens and pistils; Jalapa is the name of the city in Mexico whence the drug was first obtained. The plant is a perennial twining herb indigenous to the Mexican Andes and cultivated in Mexico, India, and to some extent in the West Indies. The plant possesses thin, horizontal underground runners, from the nodes of which the tuberous roots arise. These are usually dug in the fall, placed in nets and dried over open fires. This latter process accounts for their empyreumatic odor. Our supply comes entirely from Vera Cruz.

The early Spanish explorers who learned the cathartic properties of jalap from the natives introduced it into Europe about 1565. The exact botanical source of jalap, however, remained uncertain until 1829, and it is somewhat questionable whether the roots first introduced into Europe by the Spaniards were those of jalap.

Description.—Fusiform, irregularly ovoid or pyriform, sometimes sliced; 4 to 15 cm. in length, 4 to 10 cm. in diameter; externally dusky brown, irregularly furrowed longitudinally, sometimes wrinkled, with numerous lenticels 2 to 4 mm. in length and a few circular rootlet scars; hard, compact, resinous; internally weak to pale brown, with dark secondary, concentric cambium zones; odor distinctive and smoky; taste starchy and slightly acrid. Tubers with a specific gravity of less than 1.275 or that are whitish internally should be rejected.

Structure and Powder.—See Figures 286 and 287 and the National Formulary.

Constituents.—Resin 8 to 12 per cent; volatile oil; starch; gum and sugar; total ash, 4.33 per cent; acid-insoluble ash, 0.25 per cent. The resin contains a number of glucosides, ipurganol, a phytosterol glucoside, in colorless needles, and also found in certain *Ipomœa* species; jalapin, a mixture of acidic glucosides, also found in scammony root; also *b*-methyl æsculetin, palmitic and stearic acids, etc.

Uses and Dose.—Jalap is a hydragogue cathartic and a purgative. Average dose, 1 gm.

Jalap Resin (U. S. P. 1860 to 1936; N. F. 1936 to date) is prepared by extracting powdered jalap with an alcohol (9)-water (1) mixture. The percolate is concentrated to one-fourth the weight of drug used and is then slowly poured into water with constant stirring. The precipitated resin is washed with hot water, collected and dried.

Jalap Resin occurs in yellowish brown masses or powder. It should be free from other resins. Consult the National Formulary for properties and tests.

Jalap Resin is a hydragogue cathartic. Average dose, 125 mg.

Compound Jalap Powder (U. S. P. 1820 to 1936; N. F. 1936 to date) consists of powdered jalap, 35 parts and potassium bitartrate, 65 parts by weight.

It is very light brown. Under the microscope it displays numerous, angular, colorless fragments, mostly rectangular and with straight edges, up to 300 microns long, and very strongly polarizing with a rich display of colors (potassium bitartrate crystal fragments); numerous starch grains of jalap, usually single, and from 3 to 35 microns in diameter; occasional fragments of latex cells having yellowish brown contents, or of tracheæ with bordered pores; and rosette aggregates of calcium oxalate 10 to 35 microns in diameter.

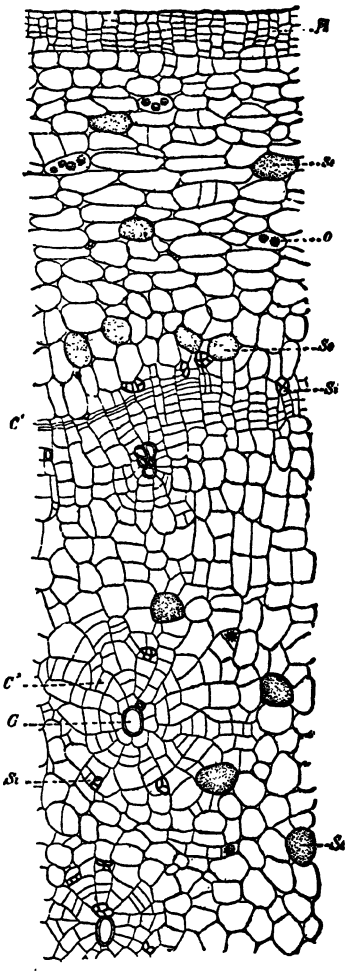


Fig. 286.—Transverse section of Jalap: *Ph*, cork cells; *Se*, resin-secretory cells; *O*, rosette aggregates of calcium oxalate; *Si*, sieve cells; *G*, tracheæ; C¹, primary cambium; C², secondary cambium. (After Meyer.)

Allied Drugs.—**Brazilian Jalap.**—During World War I several jalap substitutes were offered. One of these, known in Brazil as Batata de Purga and Batata Purgante, is the root of *Piptostegia pisonis*. It occurs in transverse circular or oval sections, from 3 to 8 cm. in diameter and 0.3 to 0.8 cm. in thickness. The cut surface is marked with several concentric rings having a pale grayish brown color and numerous dots of a translucent pale resin. It contains about 20 per cent of resin.

Resina drastica comes from Mexico and in a general way resembles Mexican scammony. The pieces represent both transverse and longitudinal sections of a root somewhat resembling Brazilian jalap but of a darker color. The cut surface is short-fibrous, due to the projections of the fibrovascular bundles.

The amount of resin is 19.2 per cent. It is of a deep lemon-yellow color and gives with ferrous sulfate a dark green color resembling true scammony resin.

Turpeth Root or Indian Jalap, is the root of *Operculina turpethum,* a plant growing in the East Indies. It contains a resin consisting chiefly of turpethin and turpethein, a glucosidal, ether-soluble, resinoid substance.

Ipomœa simulans, indigenous to the eastern slope of the Mexican Andes, yields the **Tampico Jalap,** which is more or less uniform in thickness, somewhat tortuous and without any lenticels; it contains about 10 per cent of resin, which is completely soluble in ether and resembles scammonin.

Convolvulus Pandurata, Wild Potato or Wild Jalap (U. S. P. 1820 to 1863) is the tuberous root of *Ipomœa pandurata,* a plant growing in the eastern and southern United States. It has a thick root up to 30 cm. long, contracted to a thin rhizome branch.

The root yields about 1.5 per cent of resin, which consists of two glucosides, and is powerfully cathartic. It has been replaced by other drugs.

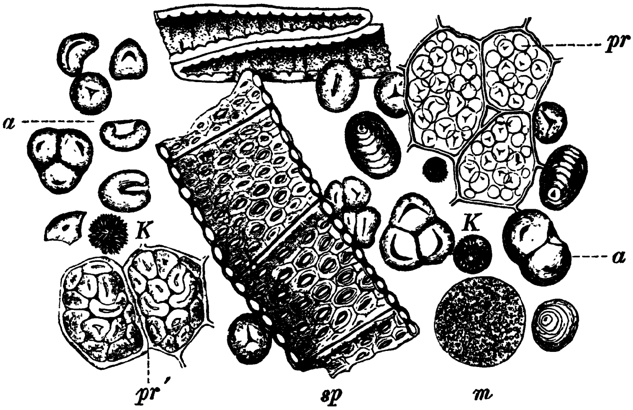


FIG. 287.—Powdered Jalap: light brown; crystals of calcium oxalate in rosettes (*K* 10 to 35 microns in diameter; starch grains (*a*) ellipsoidal and ovoid, with somewhat excentral lamellæ, from 3 to 35 microns, 1- to 3-compound and in some cases more or less swollen (*pr*); resin secretory cells (*m*) yellowish brown; tracheæ (*sp*) short, wide with simple or bordered pores; sclerenchymatous fibers few, with simple pores. Tubers deficient in resin are lighter in color and contain more starch and less calcium oxalate. (After Vogl.)

The aërial stems of the common **Morning Glory** (*Ipomœa purpurea*) contain a volatile oil and 4.8 per cent of a soft resin of which 15.5 per cent is soluble in ether.

The roots and stems of *Ipomœa fistulosa* of South America, yield 0.2 per cent of jalapin (orizabin), hexose, wax and tannin.

IPOMEA

Ipomea, Orizaba Jalap or Mexican Scammony (U. S. P. 1926 to 1936; N. F. 1936 to date) is the dried root of *Ipomœa orizabensis* Ledenois. Ipomea yields not less than 15 per cent of resin which meets the tests of Ipomea Resin, page 272 National Formulary, and not more than 3 per cent of acid-insoluble ash. *Ipomœa* is from the Greek, meaning "worm-like," in allusion to the twining stems; *orizabensis* is named after Orizaba, a city of Mexico, near where much of the drug is gathered. The plant is a perennial vine, the underground portion consisting of a fusiform root about 60 cm. long. The roots are collected, sliced, and dried in the sun.

Ipomea resin is more soluble in ether than that of jalap and more closely resembles that from Levant scammony, of which it was a common adulterant. On account of the ever-increasing scarcity of the latter, Mexican scammony finally replaced it in the United States.

Description.—Flat, transverse segments, varying from 2 to 12 cm. in diameter and from 1 to 5.5 cm. in thickness; externally light to dark brown, very deeply wrinkled; fracture tough, fibrous; internally light brown; cut surface showing concentric rings with protruding, lighter-colored fibrovascular bundles.

Structure.—A thin cork of brownish, thin-walled, narrow, tabular cells; a broad cortical layer of thick-walled, tangentially elongated, starchy parenchyma and large latex cells; zones of collateral fibrovascular bundles and broad medullary rays, alternating with zones of parenchyma and latex cells; the successive cambiums obliterated except the distinct outer one; phloem narrow, in somewhat semi-cylindrical strands outside of the xylem wedges; resin-latex cells numerous throughout the parenchyma of cortex and wood cylinder, and containing a yellowish brown, amorphous resinous mixture.

Powder.—Color pale brown to weak yellowish orange; odor distinct, somewhat aromatic; taste sweet, becoming somewhat acrid; starch grains up to 35 microns in diameter, mostly simple, also 2- to 4-compound, and usually with a central cleft; calcium oxalate crystals numerous, mostly in rosette aggregates, occasionally in rhombohedra, from 10 to 45 microns in length; fragments of resin cells; tracheæ mostly with bordered pores and associated with numerous thick-walled wood fibers with simple pores.

Constituents.—A glycosidal resin or mixture of resins, 6 to 18 per cent; volatile oil; scopoletin; 3:4-dihydroxycinnamic acid; cetyl alcohol and several fatty acids. The resin should be 70 per cent or more soluble in ether, and probably contains jalapin (a mixture of acidic glycosides); ipuranol (a sitosterol glycoside soluble in alcohol); and ipurganol (a phytosterol glycoside soluble in petroleum benzin), all of which are found, but in much different proportions in jalap resin.

Uses and Dose.—Mexican scammony root is a hydragogue cathartic. Average dose, 1 gm.

Ipomea Resin (U. S. P. 1926 to 1936; N. F. 1936 to date) is prepared by extracting powdered ipomea with an alcohol (9) water (1) mixture. The percolate is concentrated to the consistency of a syrup and then poured with constant stirring into twice its volume of hot water. The precipitated resin is washed and dried. Ipomea Resin should be free from other resins and from aloin. Consult the National Formulary for properties and tests.

Ipomea Resin is a hydragogue cathartic. Average dose, 0.2 gm.

SCAMMONY

Scammony or Scammonium (U. S. P. 1820 to 1916).

Scammony Resin or Resina Scammonii (U. S. P. 1863 to 1926, and

Scammony Root or Scammoniæ Radix (U. S. P. 1916 to 1926) are all derived from the plant *Convolvulus Scammonia* Linné, a perennial climbing herb indigenous to the countries bordering the eastern Mediterranean.

Scammony or Levant Scammony is the gum-resin obtained by incising the living root, which may attain a thickness of 5 cm. and a length of a meter. The earth is partly removed, the root crown cut off and incisions made in the root; the milky exudation is collected in shells and allowed to dry, forming circular cakes perhaps 10 cm. in diameter and about 1 cm. in thickness. The color is brownish-black, often dusty gray externally; brittle, porous, lustrous when freshly broken and translucent in thin fragments; odor peculiar, cheese-like; taste slightly acrid. At least 70 per cent of scammony is soluble in ether.

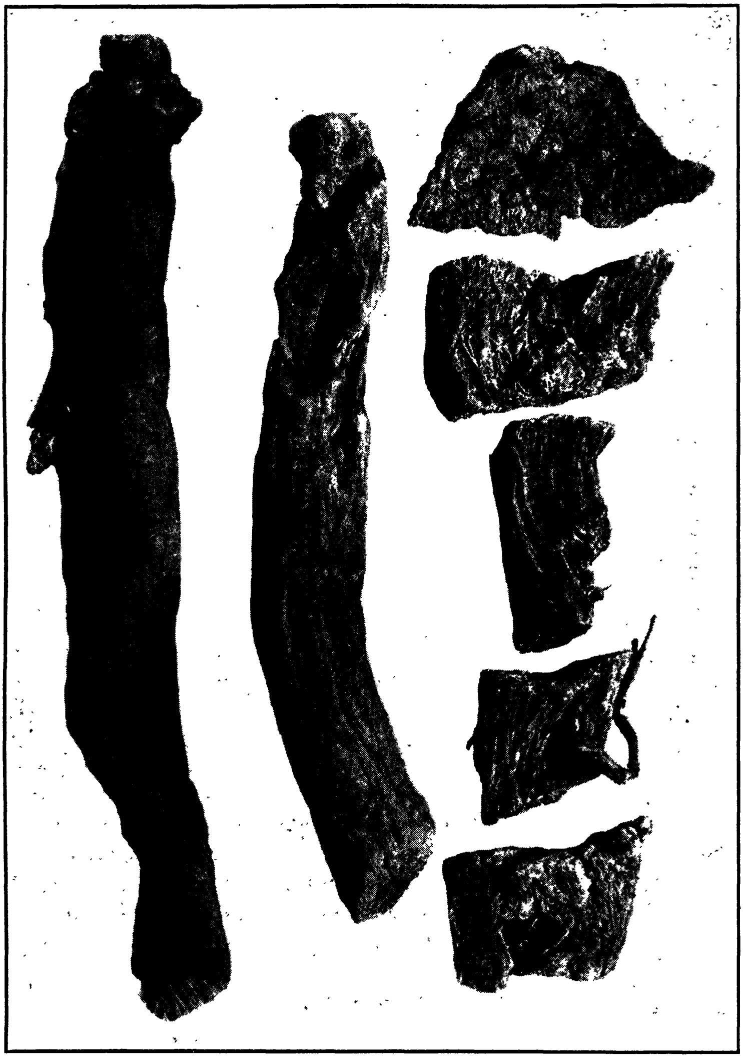


FIG. 288.—Scammony Root; Levant Scammony (*Convolvulus scammonia*) in long pieces (left), and Mexican Scammony (*Ipomœa orizabensis*) in transverse slices (right). (Photo of the commercial drugs.)

Scammony as described above was known as *virgin scammony*, but very little of it ever reached the United States. Commercial scammony has long been grossly adulterated with inorganic substances, starchy products, cheap resins, etc. It has now practically disappeared from American commerce, being replaced with ipomea resin, which rather closely resembles the genuine scammony.

Scammony Resin was early prepared in the United States by extracting the scammony gum-resin with hot alcohol, straining to remove insoluble impurities, evaporating the resinous solution to a syrupy consistency, then pouring it into about twice its volume of water to precipitate the resin; this then was washed and dried. In Great Britain and Europe, scammony resin was generally prepared from the dried Scammony Root. The ground root was extracted by maceration and percolation with alcohol, the percolate reduced to a thin, syrupy consistency and the resin recovered by precipitation in water.

Because scammony was no longer available, its monograph was deleted from U. S. P. IX (1916), but monographs for scammony root and scammony resin prepared from the root were continued for one decade, until 1926, then deleted.

The yield of scammony resin from the dried root was from 4 to 18 per cent, from adulterated scammony gum-resin perhaps 50 per cent. The resin is in brownish, translucent fragments or masses, breaking with a glossy, resinous fracture; odor characteristic and agreeable. It is readily soluble in alcohol, and at least 95 per cent of it is soluble in ether (*distinction from jalap resin and ipomea resin*). It does not form an emulsion when triturated with water (*distinction from scammony gum-resin*). It is free from *guaiac* and *rosin*.

Scammony resin consists largely of scammonin, which is probably identical with the ether-soluble resin from jalap and from ipomea.

Scammony Root, Scammony and Scammony Resin are each a hydragogue cathartic. Average dose of the root, 1 gm.; of scammony, 0.4 gm.; of scammony resin, 0.2 gm.

Montpellier Scammony is the natural exudation of *Marsdenia erecta* (Fam. *Asclepiadaceæ*), a plant indigenous to southern Europe. It contains 50 to 60 per cent of starch, 10 to 21 per cent of resin and yields 11 to 18 per cent of ash.

HYDROPHYLLACEÆ, OR WATERLEAF FAMILY

This is a family of about 17 genera and 170 species of herbs and shrubs, mostly indigenous to western North America. The leaves are opposite, the flowers are regular and 5-merous, and the fruits are capsular. From the supposition that in the springtime the leaves of the plants were filled with water, the family received its name. There is no special anatomical structure on which it would seem that this might be based. The leaves differ very little in structure from those of other plants. They are bifacial and the stomata usually occur only on the lower surface, being surrounded by an indefinite number of ordinary epidermal cells. The non-glandular hairs are usually unicellular, rarely uniseriate, occasionally encrusted with calcium carbonate, or may contain a cystolith-like body. Glandular hairs are widely distributed and are of a number of distinct types.

ERIODICTYON

Eriodictyon or Yerba Santa (U. S. P. 1894 to 1905, 1916 to 1947; N. F. 1947 to date) is the dried leaf of *Eriodictyon californicum* (Hooker et Arnott) Torrey. *Eriodictyon* is from the Greek, meaning woolly, in allusion to the hairy leaves. The plant is an evergreen shrub indigenous to the mountains of California and northern Mexico. The drug is gathered in Lake County, and has long been employed by the Indians of California. It was introduced into medicine in 1875 through the efforts of Dr. Bundy.

Description.—Usually in fragments; the unbroken leaf lanceolate, 5 to 15 cm. in length, 1 to 3 cm. in breadth; apex acute; base slightly tapering into the petiole; margin unevenly serrate or crenate-dentate; upper surface weak brown to moderate olive brown, glabrous, resinous; under surface yellowish brown to weak greenish yellow; reticulate, minutely tomentose between the reticulations, midrib light yellow, prominent; petiole 5 to 10 mm. in length; texture coriaceous, brittle.

Structure.—Cells of upper epidermis somewhat papillose, the cuticle deeply striated; deep-seated, resinous glandular hairs which resemble those of the *Labiatæ,* palisade cells very narrow, from 2 to 6 rows deep, containing numerous chloroplastids; cells of loose mesophyll very few; fibrovascular tissues not strongly developed except in the midrib and more prominent veins; lower epidermal cells having undulate, polygonal walls; in addition to the glandular hairs there occur numerous 1-celled, much contorted, thick-walled, non-glandular hairs.

Stems usually show a subepidermal cork, the cells having wide lumina and thin walls; primary cortex of 10 to 20 rows of more or less rounded parenchyma cells; pericycle consisting of a nearly closed ring of bast fibers; phloem in a narrow zone outside the xylem wedges; the latter consisting of tracheæ, having narrow lumina and marked by spiral thickenings and simple pores, and associated with lignified wood fibers having bordered pores; medullary rays 1 cell in width; pith very large.

Powder.—Yellow; odor aromatic; taste balsamic and bitter, becoming sweetish and slightly acrid; non-glandular hairs numerous, unicellular, much contorted and up to 250 microns in length; glandular hairs having a one-celled stalk and a 6- to 9-celled glandular head up to 120 microns in diameter; fragments of stems with tracheæ and lignified wood fibers; parenchyma cells from pith with thick, porous, strongly lignified walls.

Constituents.—A resin consisting of pentatriacontane; cerotinic acid; formic acid; butyric acid; probably triacontane phytosterin; xanthoeriodictyol, 0.019 per cent, in golden yellow needles; priodonal; a phenol; chrysoeriodictyol, 0.009 per cent, in golden yellow tabular crystals; a volatile oil; eriodictyonon (homoeriodictyol); a tannin, giving a green color with ferric salts; sugar; fixed oil; and gum. Total ash, 6.35 per cent; acid-insoluble ash, 0.25 per cent.

Standards.—Eriodictyon contains not more than 5 per cent of its stems and not more than 2 per cent of other foreign organic matter.

Uses and Dose.—Eriodictyon is a stimulating expectorant. It is used also to disguise the bitterness of certain medicines such as quinine. Average dose, 1 gm.

BORAGINACEÆ, OR BORAGE FAMILY

This is a family of about 1550 species which are especially abundant in the Mediterranean region and extend into central Europe and Asia. The plants are mostly herbaceous, rough and hairy. The leaves are generally alternate and the inflorescence is one-sided (dorsi-ventral). The family is characterized by both glandular and non-glandular hairs. Of special importance are the unicellular cystolith-hairs (bristle hairs). Calcium oxalate occurs in the form of prisms, rosettes and microcrystals.

Anchusæ Tinctoriæ Radix, Alkanna or Alkanet (U. S. P. 1831 to 1842) is the dried root of *Alkanna tinctoria,* a perennial herb, indigenous to southeastern Europe and Asiatic Turkey and cultivated for its coloring principle.

The root is fusiform, simple, 3 to 30 cm. in length, 5 to 20 mm. in diameter; externally deep reddish purple, or maroon color, sometimes twisted, deeply furrowed, the outer layers readily separating into papery strips, the crown being frequently several-headed and consisting of the bases of the leaves which are bristly-hairy; fracture short; internally, bark thin, wood yellowish brown; odor slight; taste insipid or faintly bitter and stringent.

Alkanet contains a coloring principle, alkannin (anchurin) 5 to 6 per cent, amorphous and resin-like. It is insoluble in water, soluble in alcohol, chloroform, ether and oils. The solutions in alkalis are of a deep blue color, changing to red on the addition of acids. Gawalowski separated alkannin into two acids: (*a*) alkanic acid, soluble in ether and alcohol and turning blue with alkalis; (*b*) anchuric acid, soluble in benzene and turning green with alkalis. Alkanet may be adulterated with Syrian alkanet, the root of *Macrotomia cephalotes* which is readily distinguishable. The roots vary from 20 to 40 cm. in length, 2 to 5 cm. in thickness and are many-headed and of a black-violet, somewhat metallic color. It contains a very large quantity of coloring matter, apparently equal to alkanet in tinctorial strength, and it may be a valuable substitute for true alkanet. Alkanet is used as a coloring agent. It colors fat red.

Borago, the herb of *Borago officinalis*, is used as a demulcent and diaphoretic. **Lungwort**, or **Pulmonaria**, is the roughly hairy herbage of *Pulmonaria officinalis*. It has reputed value in the treatment of bronchial affections. **Hound's Tongue** is the hairy leaves or herb of *Cynoglossum officinale*. It contains an alkaloid possessing a paralyzing effect on the central motor system. It has been used as a sedative and demulcent.

VERBENACEÆ, OR VERVAIN FAMILY

This is a family of 760 species of herbs, shrubs or trees, distributed in the tropics and sparingly represented in the cooler regions. The leaves are opposite or verticillate; the flowers are irregular, having a bilabiate or irregular corolla and didynamous stamens; the fruits are either drupe-like or somewhat capsular, consisting of 2 to 4 nutlets. The stems are not infrequently quadrangular in section. The tracheæ and wood fibers usually have simple pores. The stomata are surrounded by a number of ordinary epidermal cells; occasionally they possess 2 subsidiary cells which are distributed transversely to the pore. Calcium oxalate occurs in the form of small acicular or prismatic crystals. The glandular hairs have a unicellular or uniseriate stalk, the head being composed of 6 to 8 cells. A number of types of non-glandular hairs occur in the various genera of this family. An anomalous structure is developed in some of the lianes.

Verbena or American Blue Vervain (N. F. 1916 to 1926) is the dried overground portion of *Verbena hastata*, a perennial herb, growing in moist meadows throughout the central and eastern United States. The plant is gathered at the time of flowering, during the summer and should be carefully dried and preserved. The stems are quadrangular, attaining a length of one meter or more and from 1 to 6 mm. in diameter; externally reddish brown, longitudinally wrinkled and having a deep furrow between the ribs, roughly puberulent throughout; internally yellowish white with a thin brown bark, a yellowish white quadrangular wood and a hollow pith. Leaves opposite, long petiolate, from 4 to 15 cm. in length and 0.7 to 4 cm. in width; lanceolate or oblong-lanceolate, summit acute; tapering; base rounded, inequilateral; margin sharply serrate; upper surface greenish brown, glabrous; lower surface purplish green, roughly puberulent, with a prominent mid-rib; petioles 1 to 3 cm. in length, slender and puberulent; odor distinct; taste bitter. Verbena contains a glucoside, verbenalin, which crystallizes in needles and is apparently non-toxic. Also a bitter principle, tannic acid, emulsin and invertin. Verbena is a diaphoretic and expectorant.

Lippia Mexicana, Orosul, Regaliz de Cuba, is the dried leaf of *Lippia dulcis*, a trailing shrub, widely distributed in tropical America. The leaves are gathered at the time of the flowering of the plant and carefully dried.

The leaves when entire are ovate-lanceolate, petiolate, acute or acuminate, margin coarsely serrate; olive-green to greenish brown, glandular-hairy, midrib and veins prominent; petioles from 5 to 10 mm. in length; odor aromatic; taste sweetish, terebinthinate and slightly pungent.

The powder has numerous, long-pointed, unicellular, thick-walled hairs up to 300 microns in length, each containing a cystolith at the base; glandular hairs with short stalks and a 6- to 8-celled head, the latter up to 30 microns in diameter and with nearly colorless contents; epidermal cells wavy in outline; stomata elliptical, under 35 microns in length, and with the neighbor cells transverse to the pore.

The drug contains a volatile oil containing a camphor, lippiol; tannic acid, colored greenish with ferric salts; and a yellow coloring principle resembling quercetin. The drug is a demulcent and an expectorant.

Lippia Scaberrima, an aromatic drug of South Africa, is reputed to possess remarkable hemostatic properties. The drug contains about 0.25 per cent of a volatile oil; a crystalline alcohol lippianol; two yellow crystalline substances; a glucosidal substance; and a number of acids and esters.

Tonga (N. F. 1926 to 1936) is a mixture of about equal parts of the bark of *Premna arborea* and of the root of *Epipremnum pinnatum* (Fam. *Araceæ*), both of which are found growing in Fiji, Tonga and other Malaysian Islands. The mixture has been long employed as a medicine by the natives of the Fiji Islands where it is known as Yoro or Awalho. The bark occurs in small chips or quills up to 3 mm. in thickness; outer surface brownish with numerous prominent, irregular longitudinal ridges, some of which are of a pale yellow color, giving the surface a striated appearance; fracture hard and short. The root is in cylindrical pieces up to 26 mm. in thickness; outer surface light yellowish brown to dark brown with the light yellowish cork partially exfoliated; numerous root-scars or root remains along one surface; internally very fibrous and tough. Taste slight; odor slight.

Powdered tonga is dark brown; and contains spiral or scalariform tracheæ with lignified walls; numerous simple to many-compound starch grains; numerous fragments composed of long, lignified fibers with thick porous walls associated with rectangular medullary ray cells with lignified walls and large simple pores; fragments composed of starch-bearing parenchyma associated with thick-walled stone cells with simple or branching pores or non-lignified fibers, the latter frequently branched and resembling two parallel fibers, one longer than the other, united near the middle by a short connecting portion, the whole structure with a continuous lumen; numerous fragments of cork tissue, some of which are composed of cells with lignified walls; calcium oxalate in crystal fibers or in rosettes, the latter up to 95 microns in diameter.

The total ash yield is about 7 per cent. Tonga is claimed to be an anodyne.

LABIATÆ, OR MINT FAMILY

This is a large family of herbs and shrubs, comprising 170 genera and about 3000 species and widely distributed. There are about 40 different genera of the *Labiatæ* represented in the United States. They are characterized by having square stems, opposite leaves, bilabiate flowers and small, indehiscent fruits consisting of 4 nutlets. The Labiate plants bear characteristic glandular hairs consisting of a short, unicellular stalk and a glandular head of 6 to 8 cells; in the mature hairs the upper cuticle is raised like a bladder, due to the great accumulation of volatile oil. They are usually found on the under side of the leaf in depressions in the epidermis and to some extent on the petioles, stems and calyx, but not on the other parts of the flower or the fruit. Non-glandular hairs occur in a number of specific forms. In the stomata the subsidiary cells lie transverse to the pore. Calcium oxalate is secreted in the forms of small needles or short rods, rarely as rosettes. The tracheæ and wood fibers have simple pores. There is a strong development of subepidermal collenchyma, especially in the angles of the stems and branches. A secondary development of the fibrovascular bundles occurs in the older stems of *Thymus*.

VOLATILE OILS

Volatile oils are odoriferous principles found in various parts of certain plants; they evaporate when exposed in the air at ordinary temperatures. They may be formed directly by the protoplasm, or through decomposition of a layer of the cell wall (the resinogenous layer), or by the hydrolysis of glucosides. Volatile oils usually occur in special secretory containers; these may be modified ordinary cells, more elaborate tubes, intercellular spaces, glandular hairs, or other complex structures. Volatile oils, as obnoxious agents to animals, may prevent destruction of the plant; or, as attractive agents to insects, may aid in cross fertilization of the flower.

In the Conifers, volatile oils may occur in all of the tissues. In the rose they occur in appreciable quantities only in the petals; in cinnamon only in the bark and the leaves; in the Umbels in the pericarp of the fruit; in the Mint in glandular hairs on the leaves and stems; in the orange, one kind of oil in the petals of the flowers, and another kind in the rind of the fruit.

Volatile oils do not leave a permanent oily mark on paper; they possess characteristic odors; they are characterized by high refractive indices; most of them are optically active and the specific rotation is often a valuable diagnostic property. As a rule volatile oils are immiscible with water, but are soluble in most organic solvents.

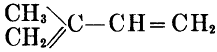
Volatile oils are usually obtained by steam distillation of the plant parts containing the oil, the oily layer separating from the water in the condensed distillate. Glucosidic volatile oils (bitter almond oil, mustard oil) are obtained by enzymic action and subsequent distillation. A few volatile oils (lemon, bergamot, etc.) cannot be distilled without decomposition and these are obtained by expression or other mechanical means.

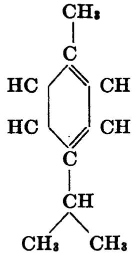
Volatile oils are usually very complex in composition and usually are deteriorated by exposure to heat, light and air. They should be kept in tightly stoppered, well-filled, amber bottles in a cool, dark place.

Chemistry of the Volatile Oils.—In only a very few cases, such as oil of mustard and oil of wintergreen, do volatile oils consist of a single chemical compound in a state of comparative purity. In most cases they are mixtures containing compounds of diverse types. These compounds may be separated in various ways, i. e.: (*a*) low temperatures (thus crystallizing out compounds); (*b*) fractional distillation; (*c*) fractional crystallization from poor solvents; (*d*) compounds with free acidic groups may be removed with sodium carbonate; (*e*) basic compounds may be removed with hydrochloric acid; (*f*) phenols with sodium hydroxide; (*g*) aldehydes with sodium bisulfite, etc.

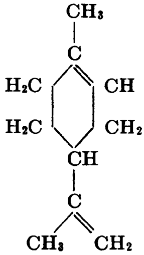
Classification of the volatile oils may be according to their principal chemical constituents. Because of the variable and diverse types of compounds often found in volatile oils, the assignment of an oil to a definite place in such a classification may be difficult.

The classification here given is based upon eight major groups, viz.:

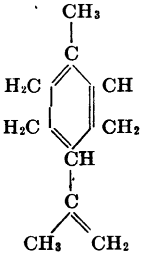
1. **Hydrocarbons.**—Most volatile oils consist largely of terpenes which are isomeric hydrocarbons having the molecular formula $C_{10}H_{16}$. Closely related are the sesquiterpenes, $C_{15}H_{24}$ and the diterpenes, $C_{20}H_{32}$. The most common terpenes are limonene and pinene (page 109), limonene probably being the most widely distributed of the monocyclic terpenes. The monocyclic terpenes are closely related to the aromatic hydrocarbon cymene (p-methyl-isopropylbenzene) and some authors believe that the naturally occurring monocyclic terpenes are derivatives of cymene. There is also a current theory that terpenes and sesquiterpenes may be produced by the polymerization of two or three molecules of the simple unsaturated hydrocarbon, isoprene,  $\begin{matrix}CH_3\\CH_2\end{matrix}\!\!>C-CH=CH_2$



Cymene

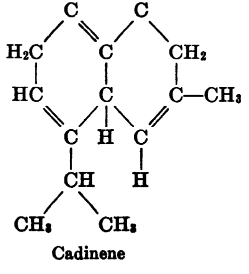


Limonene



Isoprene
(2 mols.)

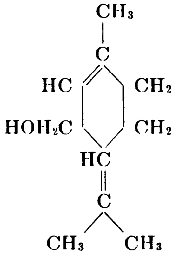
In addition to limonene which occurs in citrus oils and in caraway oil, other important monocyclic terpenes are terpinolene (coriander oil), alpha-terpinene (coriander, origanum and cardamom oils) and alpha-phellandrene (fennel and eucalyptus oils). Pinene (page 109), a dicyclic terpene, is found in many conifer oils, as are other dicyclic terpenes such as sabinene (savin oil) and thujene. Acyclic terpenes are rather rare but ocimene (ocimum oil) and myricene (myrica oil) may be cited as examples. Both have the empirical formula $C_{10}H_{16}$. Cadinene



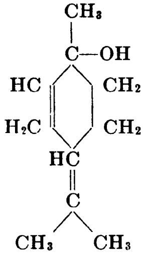
Cadinene

occurring in oil of cubeb, oil of cade and galbanum, is a typical sesquiterpene. Other examples of sesquiterpenes are zingiberene from ginger oil and selinene from celery oil.

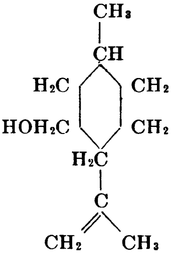
2. **Alcohols.**—Alcohols occurring in volatile oils may be classified into (*a*) acyclic alcohols, (*b*) terpene alcohols, and (*c*) sesquiterpene alcohols. Methyl, ethyl, isobutyl, isoamyl, hexyl and the higher aliphatic alcohols are known to occur in volatile oils, but since they are soluble in water they are washed away in the process of steam distillation. Many natural oils, however, contain acyclic alcohols that appear to be terpene derivatives except that the six-carbon ring is broken at one point. Among the more important of these are geraniol, linalol and citronellol.



Geraniol

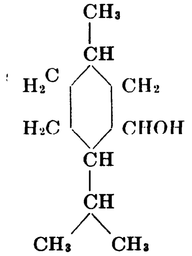


Linalol

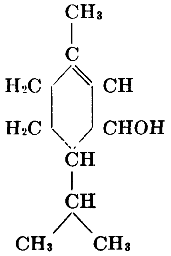


Citronellol

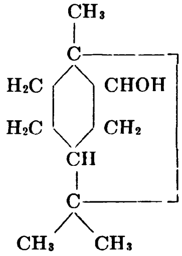
Among the more important terpene alcohols are menthol (from peppermint), piperitol (from eucalyptus) and borneol (a dicyclic terpene alcohol from Borneo camphor).



Menthol



Piperitol

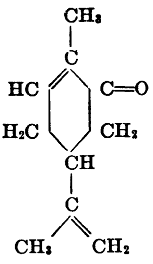


Borneol

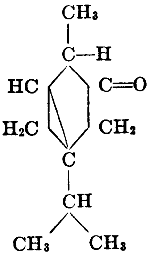
Sesquiterpene alcohols include the santalols (sandalwood oil) and zingiberol.

3. **Aldehydes.**—Aldehydes occurring in volatile oils may be divided into acyclic and cyclic. Included among the former are citral (geranial), the aldehyde corresponding to geraniol (see above), and citronellal, the aldehyde corresponding to citronellol. The aromatic aldehydes include benzaldehyde (bitter almond oil), cinnamic aldehyde (cassia oil) and vanillin (vanilla, benzoin, tolu and Peru balsams) and cuminic aldehyde (cumin seed) which is p-isopropyl-benzaldehyde).

4. **Ketones.**—Ketones occurring in volatile oils may be divided into (*a*) monocyclic terpene ketones including menthone (pennyroyal, peppermint), carvone (spearmint, caraway), piperitone (eucalyptus) and pulegone (hedeoma); (*b*) dicyclic ketones including thujone (thuja, tansy, wormwood and sage), and camphor, and (*c*) non-terpene ketones such as irone (violet, orris root).

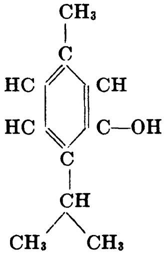


Carvone

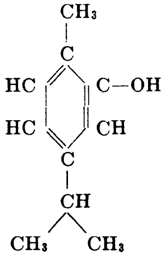


Thujone

5. **Eugonol Phenols.**—Thymol and carvacrol are the most important phenols occurring in volatile oils; Eugenol occurs in clove oil, allspice oil, and other oils: thymol and carvacrol occur in thyme oils, monarda oils, etc.



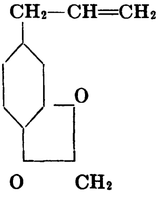
Thymol



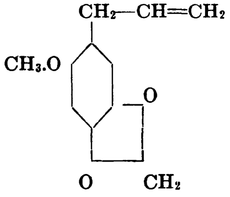
Carvacrol

6. **Phenolic Ethers.**—A number of phenolic ethers occur in volatile oils, of which the following more important examples may be mentioned: anethole from anise and fennel, and safrole from sassafras, camphor oil and Japanese star anise.

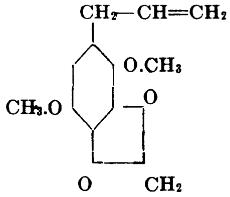
Derivatives of safrole are also often found in volatile oils. Notable among these are myristicin (methoxy safrole) from nutmeg and parsley, and apiole (dimethoxy safrole) from parsley and East Indian dill.



Safrole

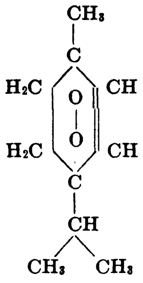


Myristicin

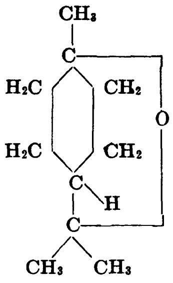


Apiole

7. **Lactones and Oxides.**—Coumarin (page 343), the lactone of coumarinic acid (o-hydroxy-cinnamic acid) occurs widely throughout the Family *Leguminosæ*. Ascaridol (page 234), a dioxide of cymene, is the active constituent of chenopodium oil. Cineol is found in several volatile oils and has been called eucalyptol (page 451) from its occurrence in eucalyptus, and cajuputol (page 452) from its occurrence in cajuput. Coumarin is a lactone, while ascaridol and cineol are oxides.



Ascaridol



Cineol

8. **Esters.**—A wide variety of esters occur in volatile oils, most common among which are the acetates of terpineol, borneol and geraniol. It is common practice to age perfumes to permit esterification to take place and thus improve bouquet. Other examples of esters in volatile oils are allyl isothiocyanate in oil of mustard and methyl salicylate in oil of wintergreen.

Microchemistry of the Volatile Oil Drugs.—Many of the above-named compounds may be isolated from the powdered vegetable drugs containing them by (*a*) microdistillation, (*b*) microsublimation, or (*c*) extraction with a solvent. Some of them may be crystallized directly on the slide (camphor, menthol, thymol) and some may be identified by crystalline compounds obtained with reagents; thus semi-carbazones and phenyl-hydrazones may be made from the aldehydes and ketones directly on the slide; sodium hydroxide forms crystalline compounds with the phenols; dihydrovanillin results from the reaction between vanillin and ferric chloride, and many others. Color reactions are also valuable in identifying the micro-isolated compounds.

THE MINTS

Peppermint (U. S. P. 1820 to date) consists of the dried leaf and flowering top of *Mentha piperita* Linné. *Mentha* is from the Greek *Mintha,* the name of a nymph mythically metamorphosed into this plant; *piperita* is from the Latin *piper,* pepper, alluding to the aromatic and pungent taste of peppermint.

The plant is a perennial herb indigenous to Europe and naturalized in the northern United States and Canada. It is extensively cultivated in Michigan, Oregon and New York, see Figures 289 and 292. The plants are propagated by rhizome cuttings. When in flower they are cut with a mowing machine, raked into windrows, dried for a few hours in the sun and hauled to the still house. If the plant is to be used as a drug it is carefully dried and preserved. Several varieties of peppermint are cultivated in the United States. Peppermint was described by John Ray in his *Historia Plantarum* (1704). It was extensively cultivated in England as early as 1750.

Description and Structure.—See Figures 290 and 291.

Constituents.—Volatile oil, about 1 per cent, resin and tannin.

Standards.—Commercial dried peppermint usually consists of the dried herb, though it should contain not more than 2 per cent of stems over 3 mm.

in diameter. It loses some volatile oil during drying and more during storage; the usual commercial sample has suffered 95 per cent deterioration and yields no volatile oil upon steam distillation, though the distillate water may be aromatic.

Uses and Dose.—Peppermint is a carminative, a stimulant and a nervine. As a medicine, it has been largely replaced by peppermint oil.

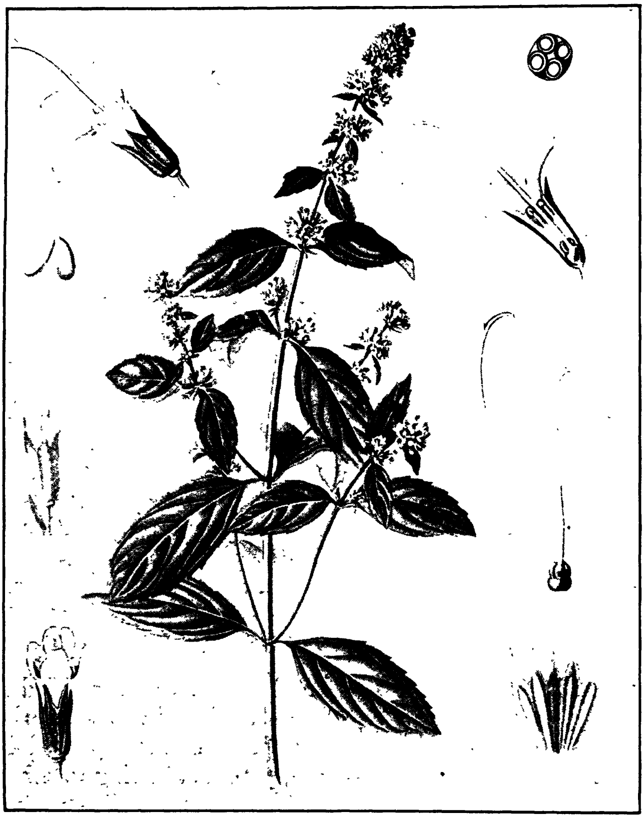


Fig. 289.—*Mentha piperita:* showing flowering stem; flower; flowers in longitudinal section, exhibiting the calyx and pistil and the gamapetalous corolla and stamens. (After Köhler.)

Peppermint Oil (U. S. P. 1820 to date) is the volatile oil distilled with steam from the fresh, overground parts of the flowering plant of *Mentha piperita* Linné, rectified by steam distillation and neither partially nor wholly dementholized. It yields not less than 5 per cent of esters, calculated as menthyl acetate, and not less than 50 per cent of total menthol, free and as esters.

America produces about 350,000 pounds of peppermint oil annually, the greater portion of which is produced in southern Michigan and northern Indiana, although some is produced in Oregon and in Wayne County, New York. Japan, Manchuria, England, France, Italy, Germany and Russia also produce mint oils.

Description.—Peppermint Oil is a colorless liquid having a strong odor of peppermint, and a pungent taste, followed by a sensation of cold when air is drawn into the mouth. Consult the U. S. Pharmacopœia for constants and tests.

Constituents.—American peppermint oil contains from 50 to 78 per cent of free menthol and from 5 to 20 per cent combined in various esters. It also contains acetaldehyde, isovaleraldehyde, acetic acid, valeric acid, pinene, phellandrene, cineol, *l*-limonene, menthone, menthyl acetate, menthyl isovalerate, menthyl ester, the lactone cadinene, amyl alcohol and dimethyl sulfide.

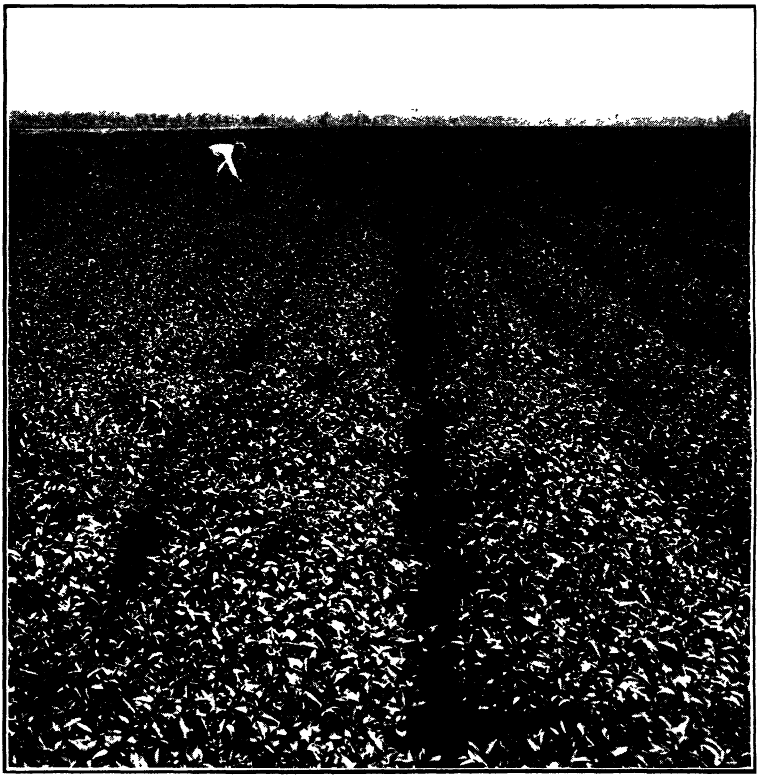


Fig. 290.—Rows of Peppermint a mile long at Mentha, Michigan.

English peppermint oil is very highly prized on account of its fine aroma and pleasant taste. It consists of 50 to 60 per cent of free menthol, 3 to 14 per cent of menthol combined as esters and 9 to 12 per cent of menthone, a substance capable of being transformed into menthol. This oil also contains phellandrene, limonene, cadinene, acetic acid and isovaleric acid.

Purity.—Peppermint oil should be free from dimethyl sulfide found in nonrectified peppermint oils; from *Mentha arvensis* oil, and from dementholized or impure peppermint oil.

Uses and Dose.—Oil of peppermint is a carminative, a stimulant and a counterirritant. It is used to a considerable extent as a flavor for confectionery and especially for chewing gum. Average dose, 0.1 cc.

Japanese Peppermint Oil or Mentha Arvensis Oil is obtained by steam distillation from *Mentha arvensis piperascens*. The oil is considerably higher in

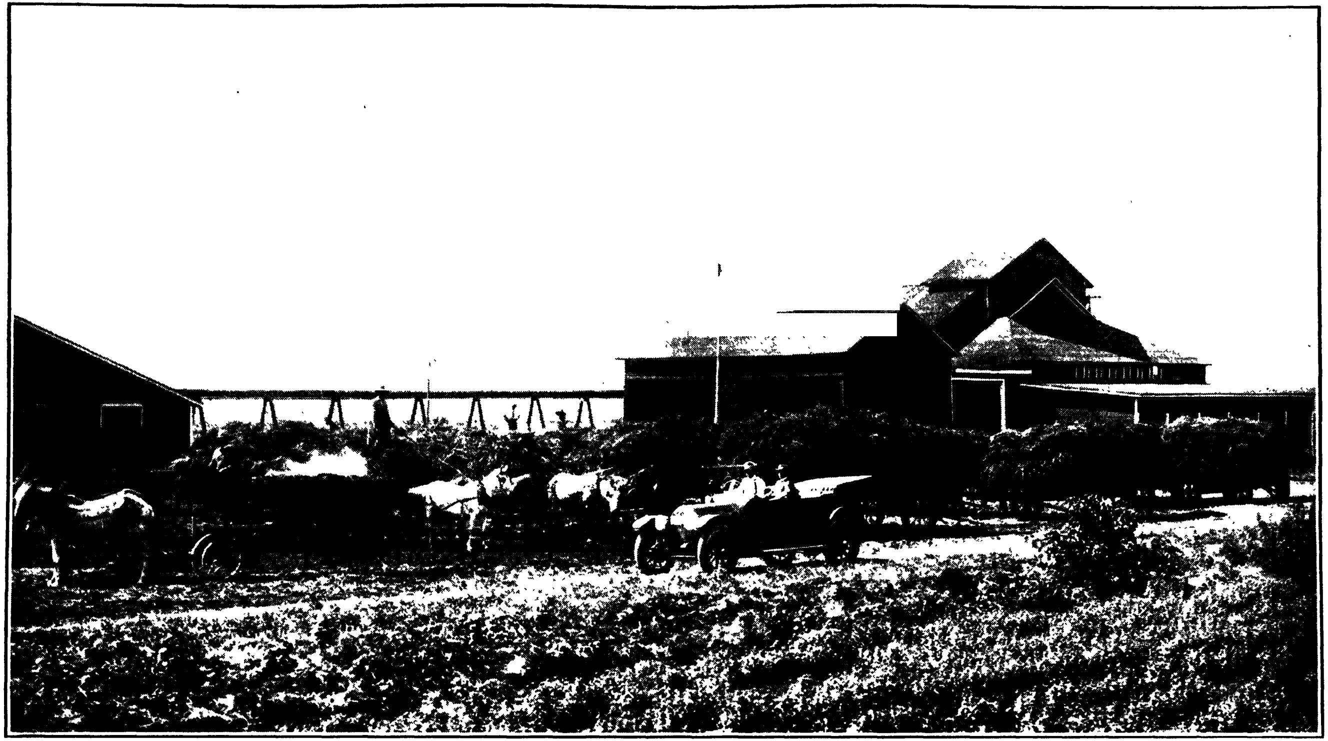


FIG. 291.—Peppermint ready for distillation. Note a steaming load of "spent" mint just from the still at the left. Mentha, Michigan.

menthol, but inferior to peppermint oil in flavor. It is therefore solely employed as a source of menthol. The plant is indigenous to Japan and is the source of Japanese Menthol exported in large quantities before the war. Several years ago the plant was introduced into southern California and more recently into Brazil, both areas now producing considerable menthol.

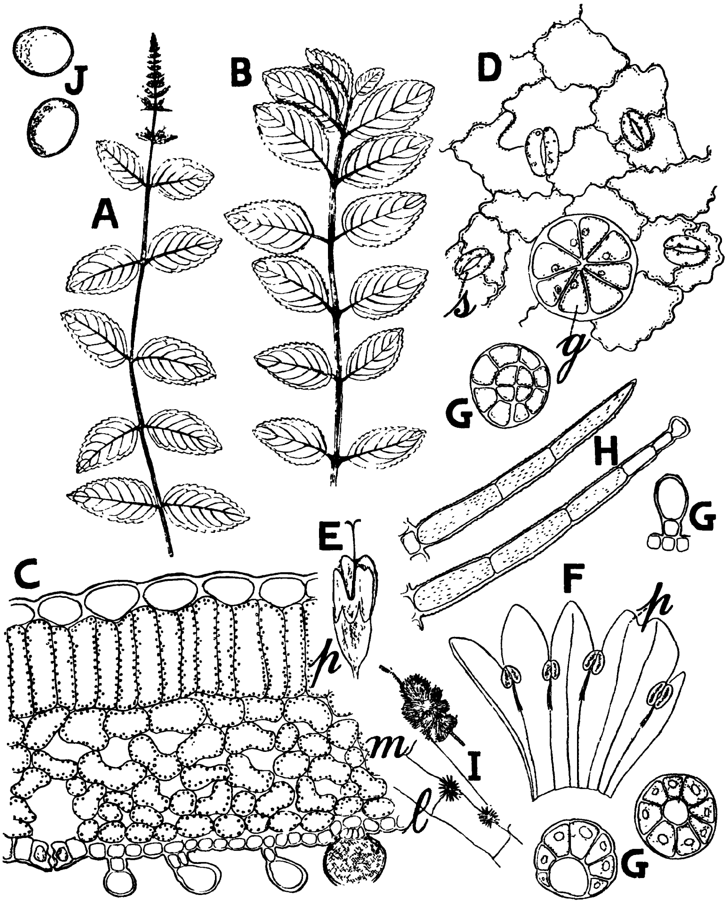


FIG. 292.—Peppermint: *B*, the quadrangular, purplish green stem, 1 to 3 mm. in thickness, and the ovate-lanceolate, opposite leaves, 1.5 to 8 cm. in length, with acute apex, acute or rounded base, sharply serrate margin, dark green, nearly glabrous upper surface and glandular pubescent, light green under surface. *C*, Transverse section of leaf showing palisade parenchyma (*p*), loose mesophyll (*m*), and lower epidermis with stoma and glandular hairs. *D*, Lower surface of leaf in surface view showing the wavy-walled epidermal cells, the numerous stomata (*s*) and glandular hairs (*g*), with a 1- or 2-celled stalk and 1- to 8-celled head containing volatile oil and occasionally crystals of menthol which refract polarized light. Spearmint (which in structure closely resembles Peppermint): *A*, portion of flower stem; note that the leaves are nearly sessile. *E*, Flower with tubular, equally 5-toothed, purplish, glandular-punctate calyx about 2 mm. in length; the outspread corolla (*F*) and 4 erect, adnate, included stamens; in peppermint the corolla is regularly 4-lobed; in spearmint the posterior lobe has an extra cleft (*p*). *H*, Nonglandular, uniseriate hairs. *G*, Short-stalked, glandular hairs set in depressions in the epidermis. *I*, Sphærites of a carbohydrate found in the corolla and style. *J*, Smooth pollen grains about 35 microns in diameter.

Menthol, $CH_3.C_6H_9.OH.C_3H_7$, (U. S. P. 1894 to date) is an alcohol obtained from oil of peppermint or other mint oils or prepared synthetically. Menthol may be levorotatory (*l*-Menthol from natural or synthetic sources) or racemic (*dl*-Menthol, produced synthetically).

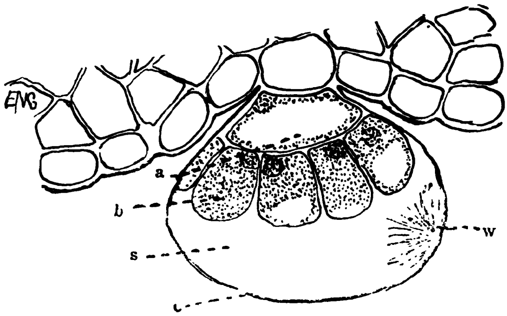


FIG. 293.—Glandular hair from leaf of Peppermint, showing a many-celled gland; *s*, secretion cavity containing Peppermint oil and crystals of Menthol (*w*); *c*, much distended cuticle; *b*, secretion cells; *a*, short stalk. (Drawing by E. N. Gathercoal.)

Menthol is usually prepared from Japanese peppermint oil by refrigeration (−22° C.) during which the menthol crystallizes. The liquid portion is poured off, and the crystallized menthol pressed between filter papers and subsequently purified by recrystallization. Synthetic racemic menthol is produced by hydrogenation of thymol.

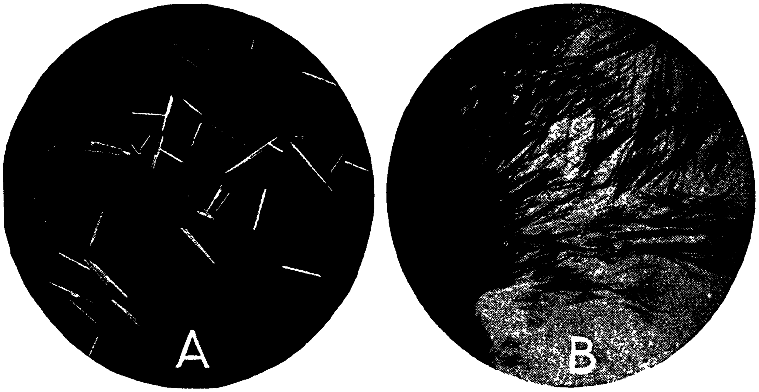


FIG. 294.—Menthol: *A*, individual crystals obtained by sublimation; *B*, the commonly occurring aggregates of very fine needles.

Menthol occurs in colorless, hexagonal crystals, usually needle-like, having a strong, peppermint-like odor. Menthol should be free from wax, paraffin, inorganic substances and thymol. Consult the U. S. Pharmacopœia for constants and tests. Menthol may be readily microsublimed.

USES AND DOSE.—Menthol is mostly employed externally on the skin or mucous membrane as an antiseptic, a local anesthetic, and a stimulant; internally it has a depressant effect on the heart. Average dose 60 mg.

Spearmint (U. S. P. 1820 to date) consists of the dried leaf and top of *Mentha spicata* Linné (*Mentha viridis* Linné). *Spicata* is from the Latin *spica* meaning a spike, and refers to the arrangement of the flowers. The plant is a perennial herb closely resembling peppermint, indigenous to Europe and naturalized and cultivated in various parts of North America. Spearmint is extensively cultivated in Michigan and to some extent in Oregon and New York. The plant appears in many of the old Herbals and its mention in early medieval lists demonstrated that it was cultivated in the convent gardens of the ninth century.

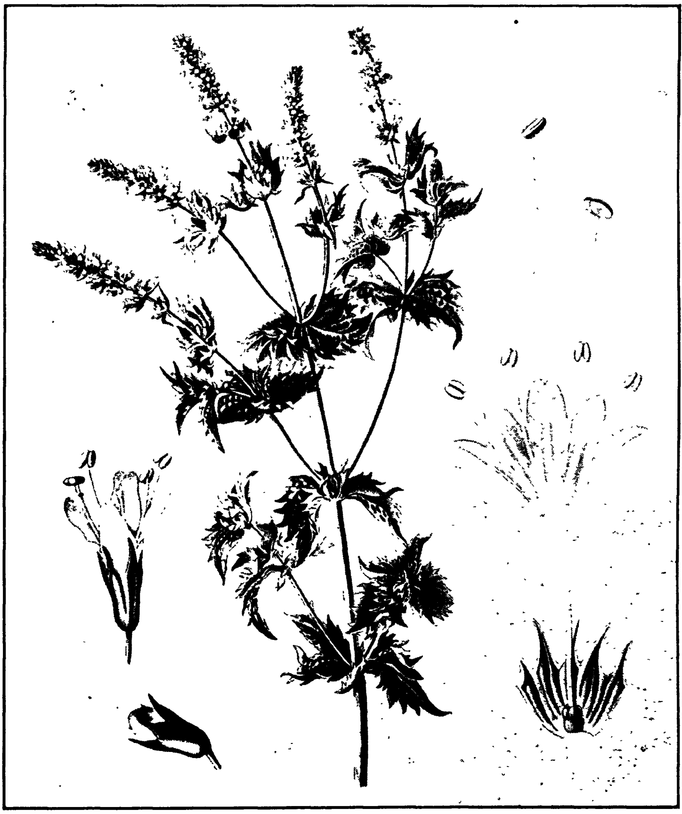


Fig. 295.—Mentha spicata. (After Köhler.)

Description.—Closely resembling peppermint (see Figs. 289 to 293), but the stems are usually more purple, the leaves sessile or nearly so, inflorescence either in slender, interrupted cylindrical spikes or crowded lanceolate spikes and the bracts are somewhat longer (7 to 10 mm.) (see Fig. 295); odor and taste aromatic, characteristic, the taste not being followed by a cooling sensation.

Powder.—Green. Closely resembling the powder of peppermint except the absence of crystals from the globular heads of the glandular hairs.

Constituents.—Volatile oil, about 0.5 per cent, resin and tannin.

STANDARDS.—Spearmint contains not more than 2 per cent of stems over 3 mm. in diameter, or other foreign organic matter.

USES AND DOSE.—Spearmint is a carminative, a stimulant and a nervine. Average dose, 4 gm.

Spearmint Oil (U. S. P. 1820 to date) is the volatile oil distilled with steam from the fresh, overground parts of the flowering plant of *Mentha spicata* Linné (*Mentha viridis* Linné). It yields not less than 50 per cent, by volume, of carvone ($C_{10}H_{14}O$). Most of our supply of spearmint oil is produced in southern Michigan in much the same way as oil of peppermint is produced.

Spearmint Oil is a colorless, yellow or greenish yellow liquid, having the characteristic odor and taste of spearmint. Consult the U. S. Pharmacopœia for constants and tests.

CONSTITUENTS.—Oil of spearmint contains from 45 to 60 per cent of carvone, 6 to 20 per cent of alcohols, 4 to 20 per cent of esters and terpenes, chiefly *l*-limonene and possibly *l*-pinene. The constituent giving the oil its characteristic odor is not known, although it has been attributed to the alcohols and esters present. Of the alcohols, dihydrocarveol has been found in the American oil, dihydrocuminic alcohol in the German oil, and linalool in the Russian oil.

The carvone present is *l*-carvone and is optically isomeric (not identical) with the *d*-carvone found in oil of caraway and oil of dill.

USES AND DOSE.—Oil of spearmint is a carminative and a flavor. It is used to a considerable extent in the chewing gum industry. Average dose, 0.1 cc.

ALLIED PRODUCTS.—**Russian Spearmint Oil** is obtained from an undetermined plant and consists of 50 to 60 per cent of *l*-linalool, 20 per cent of cineol, 5 to 10 per cent of *l*-carvone and possibly also *l*-limonene.

German Spearmint Oil is obtained from *Mentha crispa*, which is regarded as a cultural variety of *M. arvensis*. The plant is sparingly naturalized in the United States from Europe. It somewhat resembles *M. piperita*, but is distinguished by its cuspid, irregularly dentate leaves. It yields an oil containing carvone.

THYME

Thyme or Common Thyme (N. F. 1916 to date) consists of the dried leaves and flowering tops of *Thymus vulgaris* Linné. Thyme yields not less than 1.5 cc. of volatile thyme oil from each 100 gm. of the drug.

Thymus is an ancient Greek name, meaning to sacrifice, in allusion to the sweet odor; *vulgaris*, Latin, means the common or usual kind. The plant is a small evergreen shrub indigenous to Spain and Italy, and extensively cultivated in Germany, France and England for centuries, and also in the United States. The drug is gathered in May or June, carefully dried and exported from Germany and France.

DESCRIPTION.—Stems quadrangular, about 15 cm. in length and up to 2 mm. in thickness; externally dusky purplish red to dusky yellowish green; pubescent; pith hollow. Leaves lanceolate or ovate-oblong, up to 6 mm. in length, and 0.5 to 2 mm. in width; apex acute; base tapering into a short petiole; margin entire and revolute; both surfaces grayish weak olive and glandular hairy, the veins prominent. Flowers in axillary whorls; calyx 9- to 12-nerved, bilabiate, the lower lip having 2 awl-shaped, linear divisions; corolla bilabiate and about 3 mm. in width; stamens 4, straight and exserted; ovary 4-parted and having a 2-cleft style; nutlets ovoid, about 0.5 mm. in diameter, finely tuberculate.

STRUCTURE.—Non-glandular hairs unicellular, or uniseriate (2 or 3 cells), sharp-pointed, straight or somewhat curved or hooked, with thick, papillose walls and up to 60 microns or more in length; glandular hairs consist of a short stalk and a unicellular head, or without a stalk and having an 8- to 12-celled secreting head, the latter being yellowish brown in color and about 150 microns in diameter, giving the leaves a glandular punctate appearance. Calyx having 6- to 8-celled uniseriate hairs, which are long-pointed, from 300 to 400 microns in length, the walls being thin and the lumina of the lower cells filled with air.

CONSTITUENTS.—A yellowish red volatile oil, from 1 to 2.6 per cent; resin, tannin and gum.

STANDARDS.—Thyme contains not more than 3 per cent of its stems over 1 mm. in diameter and not more than 2 per cent of other foreign organic matter, and yields not more than 4 per cent of acid-insoluble ash.

USES AND DOSE.—Thyme is a stimulant, a carminative and a condiment. Average dose, 4 gm.

Thyme Oil (U. S. P. 1863 to 1926; N. F. 1926 to date) is a volatile oil distilled from the flowering plant of *Thymus vulgaris* Linné or *Thymus Zygis* Linné and its variety *gracilis* Boiss. Thyme Oil yields not less than 40 per cent, by volume, of phenols.

It is a colorless, yellow or red liquid with a characteristic, pleasant odor and a pungent persistent taste. Consult the National Formulary for its constants.

CONSTITUENTS.—French and German oils show a phenol content amounting to 25 to 42 per cent, and consisting largely of thymol, together with small quantities of carvacrol. The balance of the oil consists of cymene, borneol, linalool and pinene. The phenol content of the Spanish oil, which runs between 50 to 70 per cent, is almost entirely carvacrol.

USES AND DOSE.—Oil of thyme is a stimulant, antiseptic, and antispasmodic. It is used externally in liniments. Average dose, 0.1 cc.

Thymol, $C_{10}H_{14}O$, (U. S. P. 1882 to date; in reagents, N. F. 1936 to date) may be obtained from thyme oil (*Thymus vulgaris*), from horsemint oil (*Monarda punctata*), from *Monarda didyma* oil or from ajowan oil (*Carum copticum*). The latter, an umbelliferous plant principally grown in India is probably the source of most of the commercial supply. The oil may be subjected to freezing upon which the thymol crystallizes out and may be separated and purified, or it may be treated with sodium hydroxide solution, the aqueous solution of sodium thymol being separated and decomposed with acid, thus liberating the thymol, which is subsequently purified.

DESCRIPTION.—Large colorless crystals having an aromatic thyme-like odor and a pungent taste. Consult the U. S. Pharmacopœia for properties and tests.

Thymol may be readily microsublimed. If this process is carried out slowly at a temperature of 35° C., four-sided oblique-angled plates are formed, showing an acute angle of 82 to 85 degrees.

USES AND DOSE.—Thymol is an antiseptic, a parasiticide and deodorant. It is an anthelmintic, being especially serviceable for hookworm. Average dose: antiseptic, 125 mg.; anthelmintic, 2 gm. divided into 3 doses.

Thymol Iodide (U. S. P. 1905 to 1947; N. F. 1947 to date) is a mixture of iodine derivatives of thymol, principally dithymoldiiodide, containing, when dried over sulfuric acid for eighteen hours, not less than 43 per cent of iodine. It occurs as a red-brown or red-yellow bulky powder, insoluble in water, but slightly soluble in alcohol, glycerin, carbon disulfide, paraffin oil, etc. It is used as an antiseptic in oil solutions, ointments, suppositories and dusting powders.

Monarda, Horsemint or Mountain Balm (U. S. P. 1820 to 1882) consists of the leaves and tops of *Monarda punctata* Linné. The plant is a perennial herb up to 60 cm. high, indigenous to eastern United States, southward and west to the Mississippi River.

The leaves are up to 5 cm. long, lanceolate, acute, toothed, and glandular-dotted beneath. The flowers are in small cymes in the axils and appear in late summer. The drug has a strongly aromatic odor and a warm, pungent, bitterish taste.

Oleum Monardæ or Monarda Oil (U. S. P. 1820 to 1882) is the principal active constituent. The fresh plant is steam distilled, yielding up to 0.5 per cent of oil, which is reddish or brownish in color, soluble in alcohol, crystallizing when below 5° C. It contains about 60 per cent of thymol, considerable cymene, some *d*-limonene, carvacrol and linalool. The oil is a source of thymol. It is used internally as a carminative and diaphoretic; externally in liniments as a stimulant, counterirritant and vesicant. Average dose, 100 mg.

Monarda Didyma, Bee Balm or Oswego Tea, the leaves and flowering tops of *Monarda didyma* Linné; and **Monarda Fistulosa or Wild Bergamot,** the leaves and flowering tops of *Monarda fistulosa* Linné, have both been used in domestic medicine as carminatives and stimulants. They yield volatile oils upon distillation and the oils, especially the one from Monarda Didyma, are rich in thymol.

Thymus Serpyllum, Wild Thyme, Creeping Thyme or Mother-of-Thyme consists of the dried leaves and flowering tops of *Thymus serpyllum,* a low prostrate, creeping perennial herb indigenous to Europe and northern Asia and naturalized in the United States. Commercial supplies are imported from Europe. Wild thyme yields about 0.5 per cent of a volatile oil containing carvacrol, thymol and cymene. The drug is employed as an antispasmodic in whooping-cough.

Cretan Dittany or Origanum Dictamnus consists of the dried leaves and tops of *Origanum dictamnus,* a native of the Isle of Crete in the eastern Mediterranean Sea, and is sometimes sold as thyme. The name *Origanum* is from two Greek words, meaning mountain and brightness or joy; *dictamnus* is the classical name, from Mt. Dicte in Crete, on which the plant grew luxuriously. The stems are nearly cylindrical, reddish brown, from 0.5 to 2 mm. in diameter. The leaves are broadly elliptical, light greenish gray and densely tomentose. The bracts are purplish brown and the corolla dark purple. The plant yields a volatile oil containing about 85 per cent of pulegone.

Spanish Hops or Origanum Creticum consists of the dried leaves and tops of *Origanum creticum,* and is sold for thyme. The plant is indigenous to southern Europe and consists of numerous cylindrical or somewhat quadrangular stems of a yellowish or light brown color; a number of elliptical or ovate, short-petiolate leaves, about 10 mm. in length, grayish green, glandular hairy and with 5 palmate veins; and numerous ovoid or cylindrical spikes having grayish green imbricated bracts and enclosing in fruit the ovoid nutlets; the latter being elliptical, yellowish brown, about 1 mm. in length and having the epidermal cells modified to papillæ. The plant yields from 2 to 3 per cent of a volatile oil containing from 60 to 85 per cent of carvacrol. The oil, from different sources, varies in color and in the carvacrol content.

Fever Basil or Ocimum Viride, the leaves and tops of *Ocimum viride,* a native of West Africa, yields 0.45 per cent of volatile oil which contains 52 per cent of thymol.

LAVENDER

Lavandula or Lavender Flowers (U. S. P. 1820 to 1894) consists of the dried flowers of *Lavandula vera* DeCandolle (*L. Spica* Linné, *L. officinalis* Chaix).

Oleum Lavandulæ or Lavender Oil (U. S. P. 1820 to 1894) is the volatile oil distilled with steam from the fresh flowering herb of *Lavandula vera* DC.

Oleum Lavandulæ Florum, Lavender Oil or Lavender Flower Oil (U. S. P. 1894 to date) is the volatile oil distilled with steam from the fresh flowering tops of *Lavandula officinalis* Chaix et Villars (*Lavandula vera* DeCandolle). It contains not less than 30 per cent of esters calculated as linalyl acetate.

Oil of Spike Lavender or Spike Oil is the volatile oil distilled from *Lavandula Spica* DC. (*L. latifolia* Villers).

The lavender plants are native to Italy, southern France, Spain, and northwestern Africa, cultivated in Europe north to Norway, in England and the United States (southern California). The leaves and flowers were used by the Romans to scent their baths, and the name *Lavandula* refers to the Latin *lavo,* to wash. The flowers and their oil still remain a chief toilet perfume in sachet powders, soap, bath salts, perfumes, etc. The flowers produced in the Mediterranean climates, especially on higher elevations, yield finer oil than those grown in colder climates.

Lavender Flowers are bilabiate, from 5 to 8 mm. in length, nearly sessile; calyx tubular, about 4 mm. in length, obscurely 5-toothed, prominently nerved and dark blue in color, the lower portion being somewhat grayish and hairy; the corolla about 4 mm. in length, dark blue or bluish brown, tubular, two-lipped, and with characteristic, corkscrew-like glandular hairs; odor, strongly aromatic and distinct; taste, aromatic, slightly pungent and somewhat bitter. They contain from 0.8 to 2.8 per cent of the volatile oil.

Lavender Oil is a colorless or yellow liquid, having the characteristic odor and taste of lavender flowers. The oil should be free from alcohol and acetins. Consult the U. S. Pharmacopœia for constants and tests.

CONSTITUENTS.—*l*-linalyl acetate, 30 to 45 per cent in the French oil; geraniol, linalool, limonene, a sesquiterpene, some cineol, an ester of butyric acid and possibly of valeric acid. The French lavender oils are divided into two classes: (*a*) those with more than 36 per cent of linalyl acetate, possessing the finest and most intense aroma, being produced in the southern French Alps; (*b*) those having from 30 to 36 per cent of ester. The English oils contain from 7 to 11 per cent of linalyl acetate and are especially esteemed for their distinctive odor, which is partly due to the high cineol content (20 to 30 per cent).

Spike Lavender Oil contains much less of linalyl acetate, about 35 per cent of cineol, some camphor, borneol, linalool, and probably terpineol. It is extensively used in cheap perfumery.

The lavender plants tend to hybridize and many of the hybrids produce pleasant and distinctive oils. However, so many varieties of lavender oil are confusing.

USES AND DOSE.—Oil of lavender is a mild stimulant and a carminative. It is employed to perfume and flavor pharmaceutical preparations. Average dose, 0.1 cc.

ROSEMARY

Rosemarinus or Rosemary (U. S. P. 1820 to 1894) is the dried leaves of *Rosemarinus officinalis* Linné.

Rosemary Oil (U. S. P. 1820 to date) is the volatile oil distilled with steam from the fresh flowering tops of *Rosemarinus officinalis* Linné. It contains not less than 1.5 per cent of esters calculated as bornyl acetate and not less than 8 per cent of total borneol, free and as esters (see page 536). *Rosemarinus* is from two Latin words, *Ros,* meaning dew, and *marinus,* meaning sea, and refers to its glaucus appearance.

The plant is a branched, bushy, perennial shrub attaining a height of about 1 meter, growing in France, the Dalmatian Islands, Spain and northern Africa. Although a native of southern Europe, rosemary was cultivated in English gardens even before the Norman Conquest.

Rosemary Leaves are linear to linear-lanceolate, from 1.5 to 3.5 cm. long and 2 to 4 mm. broad; upper surface dark green and glossy; lower surface gray and woolly due to the presence of branching hairs; glandular hairs of the labiate type present; midrib prominent on the lower side; margin revolute; odor aromatic, characteristic; taste pungently aromatic, camphoraceous and bitter. Rosemary contains from 1 to 2 per cent of volatile oil. Most of the present-day supply of the oil comes from France.

Rosemary Oil is a colorless or pale yellow liquid, having the characteristic odor of rosemary, and a warm camphoraceous taste. Consult the U. S. Pharmacopœia for constants, etc.

The constituents of oil of rosemary are not completely known. The oil contains from 2 to 6 per cent of esters, probably largely bornyl acetate; from 8 to 20 per cent of total alcohols of which borneol seems to predominate; about 20 per cent of cineol, and terpenes (probably pinene and camphene).

USES AND DOSE.—Oil of rosemary is a stimulant and a carminative. It is also used in liniments as a rubefacient. Average dose, 0.1 cc.

SALVIA

Salvia or Sage (U. S. P. 1842 to 1916; N. F. 1936 to date) is the dried leaf of *Salvia officinalis* Linné. It yields not less than 1.25 cc. of volatile oil from each 100 gm. of drug. *Salvia* is from the Latin *salvare,* meaning to save, and refers to its use in preserving meats. The plant is a perennial herb attaining the height of about 50 cm., indigenous to southern Europe, Germany and the United States. The leaves are gathered when the plant is in flower and carefully dried in the shade. Most of the commercial supply comes from southern Europe.

DESCRIPTION.—Oblong-lanceolate or ovate, 2 to 10 cm. in length, 1 to 2.5 cm. in breadth; apex acute; base rounded or somewhat heart-shaped, frequently lobed; margin crenulate; upper surface grayish green, densely pubescent when the leaves are young, the older leaves being nearly smooth, midrib and veins depressed; under surface light grayish green, midrib prominent, minutely reticulate and densely pubescent; petiole 1 to 4.5 cm. in length, upper side grooved, grayish purple; texture velvety, more or less pliable; odor aromatic; taste aromatic and bitter.

STRUCTURE.—Non-glandular hairs numerous, uniseriate, consisting of 2 to 5 thick-walled cells containing air. Glandular hairs of three types: (*a*) a 2- to 4-celled stalk and a small 1-celled head; (*b*) a 1-celled stalk and a 2-celled head; (*c*) without a stalk and having an 8-celled, glandular head, containing a brownish secretion. Cells of upper epidermis polygonal in surface view and thick-walled; those of lower epidermis undulate and thin walled in surface view.

POWDER.—Dark green; containing numerous characteristic non-glandular hairs, also reddish glandular hairs as described above.

CONSTITUENTS.—Volatile oil 0.5 to 2.5 per cent containing pinene, cineol, thujone, and borneol; a bitter principle somewhat resembling marrubiin; resin; and tannin, or a principle closely resembling it in its astringency and behavior with ferric salts.

STANDARDS.—Salvia yields not more than 25 per cent of crude fiber, not more than 10 per cent of total ash and not more than 1 per cent of acid-insoluble ash, and contains not more than 10 per cent of the stems of the plant and not more than 2 per cent of other foreign organic matter.

Unground salvia should contain no leaves that are broad, dark green, or with a cordate base (*other Salvia species*), and powdered Salvia should not contain stellate hairs (*Phlomis species*) or an abundance of reticulate tracheæ and crystal-bearing fibers (*Sage stems*).

USES AND DOSE.—Salvia is a stimulant, a carminative and a condiment. Due to the astringent and slightly antiseptic properties of sage, an infusion is used as a gargle. Average dose, 4 gm. It is extensively used as a seasoning agent, especially with meats, such as goose, pork and sausage. Sage Oil may be used in place of the dried powdered leaves as a condiment.

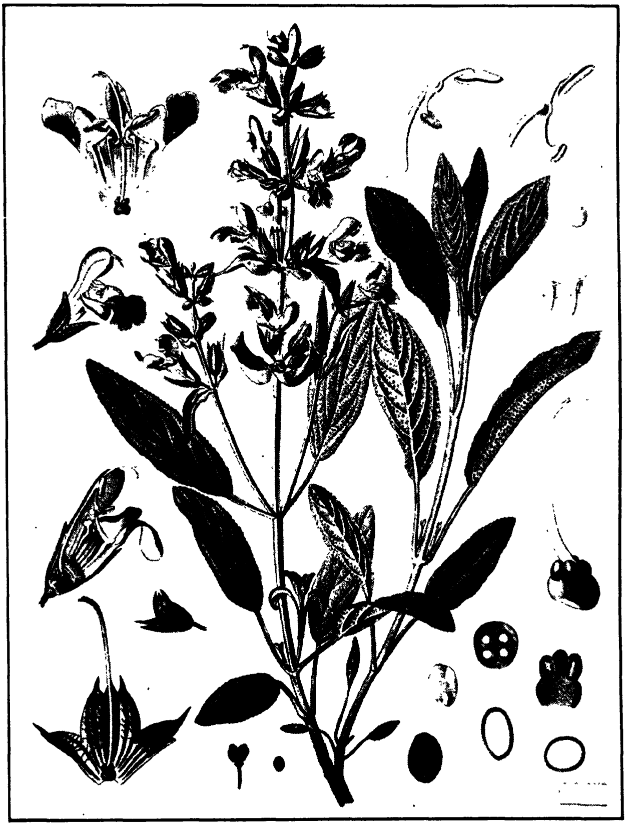


FIG. 296.—*Salvia officinalis*. (After Köhler.)

Greek Sage (*Salvia triloba*) has leaves broader and thicker, with short petioles, and with a more woolly surface than official sage leaves.

Spanish Sage (*Salvia lavandulæfolia*) has leaves considerably smaller than the official article and possessing relatively long petioles, entire margins and a cordate base. The leaves of *Salvia pratensis* are darker in color. These sages and leaves of *Phlomis* species, readily detectable by the stellate hairs, have been found as adulterants of sage.

Sclary Sage or Muscatel Sage, the dried leaves of *Salvia Sclarea* Linné, is extensively used in southern Europe. The oil of this sage has an odor of lavender, probably contains linalyl acetate, and is used in perfumery.

CATARIA

Cataria, Catnip, Catnep, or Catmint (U. S. P. 1842 to 1882; N. F. 1916 to date) consists of the dried leaves and flowering tops of *Nepeta Cataria* Linné. *Nepeta* is the ancient Latin name; *cataria* is derived from the Latin *Catus,* meaning cat, and is applied because cats are fond of the plant, eating it and rubbing themselves against it. The plant is a common perennial herb naturalized in the United States from Europe and often growing as a weed.

The leaves and tops are gathered in the late summer when the plant is in bloom, and carefully shade dried. Most of the drug comes from plants cultivated in the United States.

DESCRIPTION.—See Figure 297 and the National Formulary.

POWDER.—Light olive brown to light olive; odor, aromatic and mint-like; taste, bitter, aromatic and pungent; numerous fragments of parenchyma and palisade tissue containing green plastids; non-glandular hairs numerous, 1- to 5-celled, tapering, more or less broken, the basal cells up to 50 microns in diameter; glandular hairs with 1-celled stalk and many-celled secreting head, the latter up to 70 microns in diameter; tracheæ with spiral, reticulate, annular or simple pore markings; stomata broadly elliptical up to 30 microns in diameter; collenchyma and lignified wood-fiber bundles few.

CONSTITUENTS.—Catnep contains a bitter principle, tannin and an oxygenated volatile oil. Carefully cleaned leaves yield about 13 per cent of natural ash, stems about 10 per cent and roots about 7.5 per cent. The leaves yield about 1 per cent of acid-insoluble ash, and the stems about 0.5 per cent. The drug yields up to 1 per cent of volatile oil.

STANDARDS.—Catnep contains not more than 5 per cent of its stems over 4 mm. in diameter or other foreign organic matter, and yields not more than 2 per cent of acid-insoluble ash.

USES AND DOSE.—Cataria is used as a carminative, a stimulant, a diaphoretic and a tonic. Average dose, 4 gm.

Scutellaria or Skullcap (U. S. P. 1863 to 1916; N. F. 1916 to 1947) is the dried overground portion of *Scutellaria lateriflora* Linné. *Scutellaria* is from the Latin *scutella,* a dish, alluding to the calyx when fruiting; *lateriflora* alludes to the arrangement of the flowers on the stem.

The plant is a perennial, smooth herb, with an erect, freely branching stem attaining a height of about 65 cm., and found growing in wet places in the United States and Canada. The plant blooms from July to September when the herb should be collected.

The history of scutellaria abounds with surprising interest, and the student is referred to John Uri Lloyd's "Origin and History of Pharmacopœial Vegetable Drugs," where the story is related in a most interesting manner. A certain Dr. Van Derveer (1773) found the drug particularly useful in the treatment of rabies and considerable evidence supporting this fact has been related by Dr. Lyman Spalding (the Father of the United States Pharmacopœia). The remedy passed into the hands of an advertising charlatan named Lewis, whose notorious methods brought discredit to the drug; however, the name, mad-dog skullcap still adheres to it. The original use of the drug has been entirely lost sight of and other uses have become conspicuous.

DESCRIPTION.—Stem quadrangular, 1 to 4 mm. in diameter, yellowish green to purplish red, mostly glabrous below and hairy above. Leaves (Fig. 298) 1.5 to 3 cm. in length, 0.5 to 2.5 cm. in breadth; upper surface dark green, glabrous; under surface light green, nearly smooth; petiole 2 to 10 mm. in length. Flowers axillary and solitary above or in 1-sided racemes; calyx campanulate; corolla white or blue, about 6 mm. in length, the limb 2-lipped; stamens 4, didynamous, hairy, the anthers of the upper pair with 2 pollen sacs, the lower with one; style unequally 2-cleft and ovary deeply 4-parted. Fruit consisting of 4 ellipsoidal, distinctly tuberculate, light brown nutlets about 1 mm. in length, borne on an enlarged torus known as the gynobase, and enclosed by

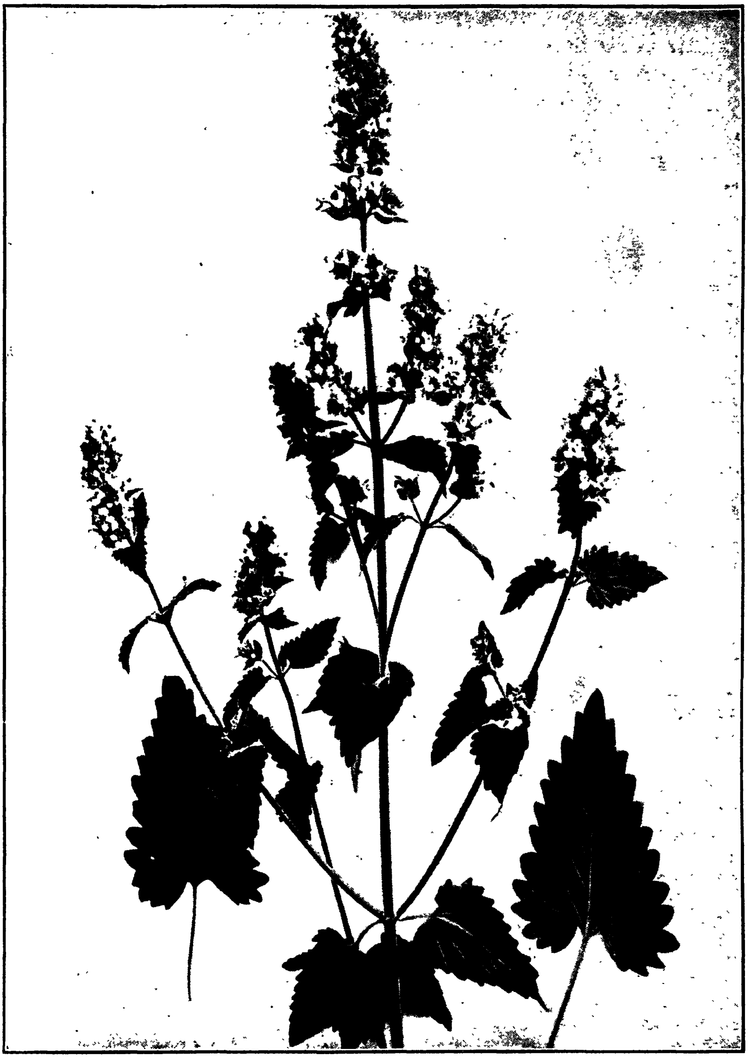


FIG. 297.—Catnip: tops, from 10 to 20 cm. long, much branched or crushed and broken; stems quadrangular, downy, up to 4 mm. in diameter; leaves opposite, the larger, petiolate, from 2 to 7 cm. long, ovate or oblong, rounded or heart-shaped at the base, pointed at the apex, pale gray-green, soft-hairy above, downy beneath, margin deeply crenate; floral leaves small, bract-like; flowers small, in dense, interrupted spikes; calyx hairy, tubular, curved obliquely and subequally 5-toothed; corolla whitish, dotted with purple, throat dilated, limb bilabiate, the upper lip erect and 2-cleft, the lower spreading and 3-cleft, the middle lobe largest, crenulate; stamens 2 pairs ascending under the upper lip, lower pair shorter. Odor faintly aromatic and mint-like; taste bitter, pungent and aromatic. (After U. S. Bureau of Plant Industry.)

the persistent bilabiate calyx, the upper part of which becomes helmet-shaped after fertilization, whence the name "Skullcap."

STRUCTURE.—See Figure 298.

POWDER.—Dusky greenish yellow; odor slight; taste bitter; non-glandular hairs long, numerous, 1- to 3-celled, the basal cell being large, broadly cylindrical and the apical cell narrow and with a sharp, frequently recurved summit; glandular hairs with a 1- or 2-celled stalk and large, glandular head, composed of 4 cells divided by vertical walls, indistinct; pollen grains nearly spheroidal or ellipsoidal, smooth and up to 25 microns in diameter; fragments of corolla colored light pink with chloral T.S.; narrow tracheæ with scalariform and reticulate thickenings or bordered pores. In *Scutellaria canescens* the non-glandular hairs are 3- to 5-celled and vary in length from 0.3 to 1 mm.; the glandular hairs have a 4-celled stalk and 8-celled head, are larger and more prominent than in *S. lateriflora;* and the stomata are narrowly elliptical (Fig. 298).

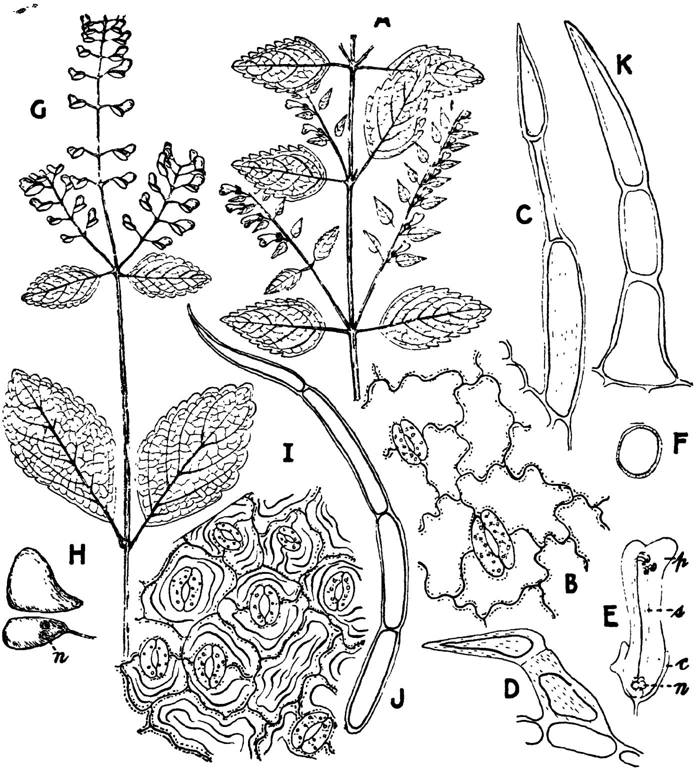


FIG. 298.—*Scutellaria lateriflora:* *A*, portion of branch showing the ovate serrate leaves and the axillary one-sided racemes. *B*, Lower surface of leaf, showing elliptical stomata. *C*, *D*, hairs from the stem and lower surface of leaf. *E*, Section of flower showing calyx (*c*), with crest on one side, 2-lipped corolla (*p*), the didynamous stamens (*s*), and 4-locular ovary (*n*). *F*, Pollen grains, 15 to 25 microns in diameter. Hairy skullcap (*Scutellaria pilosa*). *G*, Branch showing crenate leaves and helmet-shaped capsular fruits. *H*, Capsule after dehiscence showing nutlets (*n*). *Scutellaria canescens:* *I*, view of lower surface of leaf showing numerous broadly elliptical stomata and wavy cuticle. *J*, *K*, hairs from the leaf.

Constituents.—A bitter crystalline glucoside scutellarin; a small quantity of volatile oil, of which little is known. Total ash, about 7.5 per cent; acid-insoluble ash, about 0.5 per cent.

Uses and Dose.—Scutellaria is a tonic, a nervine and an antispasmodic. Average dose, 1 gm.

Western Skullcap (*Scutellaria canescens*), a plant growing west of the Mississippi, furnishes much of the drug on the market. The plant is more robust than *S. lateriflora;* the leaves are oblong, petiolate, 10 to 12 cm. in length, 3 to 5 cm. in breadth, very hairy on the under surface, with prominent veins, and crenate-dentate margins; and the flowers are large, blue and in terminal racemes (Fig. 298).

Allied Plants.—Several species of *Scutellaria* growing in the United States are sometimes substituted for the genuine drug; nearly all of these have the flowers in terminal panicled racemes. **Heart-leaved Skullcap** (*Scutellaria cordifolia*) is densely glandular pubescent, even the corolla being hairy. **Hairy Skullcap** (*S. pilosa*) is pubescent below, with numerous glandular hairs above and the corolla is nearly glabrous; **Hyssop Skullcap** (*S. integrifolia*) has linear entire upper leaves; in **Marsh Skullcap** (*S. galericulata*) the flowers occur in the axils of the nearly sessile, narrow leaves. The **European Skullcap** (*S. altissima*) has broad, ovate, glabrous leaves and terminal panicles of blue flowers.

Marrubium or White Horehound (U. S. P. 1820 to 1916) consists of the dried leaves and flowering tops of *Marrubium vulgare*, a perennial herb indigenous to Europe and Asia, and cultivated in various parts of Europe and the United States, being naturalized in waste places from Texas and Mexico to Maine and Ontario. The stems are quadrangular, yellowish or grayish green, very pubescent. Leaves broadly ovate, opposite, 1.5 to 6 cm. in length; apex obtuse; base acute or rounded; margin coarsely crenate; upper surface dark green, pubescent, veins depressed; under surface grayish green, very pubescent, veins prominent; petiole 0.5 to 3 cm. in length. Flowers sessile, in axillary clusters; calyx tubular, about 5 mm. in length; corolla whitish or light brown, about 7 mm. in length, upper lip erect, entire or bifid; stamens 4, included. Nutlets brownish black, ellipsoidal, slightly compressed, about 1.5 mm. in length, nearly smooth. Odor slight, aromatic. Taste aromatic and bitter.

Non-glandular hairs of three types are present: (*a*) Short, unicellular hairs; (*b*) long-pointed, unicellular hairs, having papillose walls; and (*c*) branched or tufted, multicellular hairs, having from 6 to 15 cells radiating from a central stalk. Glandular hairs of two types having either a short or long stalk and a 2- to 8-celled glandular head. Epidermal cells of both surfaces more or less tabular, the walls being but slightly undulate. The powder is dark green; spheroidal, spinose pollen grains, about 25 microns in diameter, are numerous.

Marrubium contains a bitter, somewhat acrid principle, marrubiin, 0.02 to 4 per cent, which forms prismatic crystals and is sparingly soluble in water; several other bitter principles; a volatile oil; a resin; and tannin. The commercial drug consists at times of *Ballota hirsuta.* Marrubium is a stimulant and a tonic; in large doses it is a diuretic and a diaphoretic.

Black Horehound, *Ballota nigra,* an herb of the Old World, naturalized in New England, possesses ovate or lanceolate, dentate-serrate, cordate, hairy leaves; flowers with a funnel-form calyx; a pale purple corolla shorter than the calyx and anthers exserted beyond the tube of the corolla. Odor disagreeable, hence the name, Fetid Horehound.

Water Horehound, *Lycopus europæus,* possesses ovate-lanceolate, lobed or divided leaves, and the calyx lobes are triangular. It has been used as an astringent, a sedative, a diuretic and a diaphoretic, especially to relieve intermittent fever.

Lycopus or Bugleweed (U. S. P. 1831 to 1882) is the herb of *Lycopus virginicus* Linné, a biennial found in shady, moist places from Canada southward to South Carolina. It grows to a height of 0.5 meter with a smooth stem; opposite, short-petioled, slender-elliptical, toothed, pellucid-punctate leaves; and with axillary clusters of purplish flowers. The drug has a mint-like odor and a bitter, somewhat aromatic taste. It contains a small percentage of volatile oil and a bitter principle.

It has been used as an astringent and a sedative and it reduces the pulse rate. It is now rarely used in medicine.

Hedeoma or American Pennyroyal (U. S. P. 1831 to 1916) consists of the dried leaves and flowering tops of *Hedeoma pulegioides*, an annual herb indigenous to the eastern and central United States and Canada. Pennyroyal should be collected in July or August and dried.

The stem is quadrangular, 1 to 2 mm. in diameter, light or reddish brown, with numerous spreading hairs. The leaves are elliptical or ovate, opposite, 15 to 35 mm. in length, base tapering into the petiole; margin remotely serrate; upper surface dark green; under surface light green, pubescent, glandular-hairy; inflorescence in 6-flowered axillary whorls; calyx tubular, about 5 mm. in length, pubescent; corolla about the size of the calyx, purplish, pubescent; fertile stamens 2, exserted, ascending, the sterile upper pair rarely with anthers. Nutlets nearly spheroidal or ovoid, about 0.5 mm. in diameter; odor strongly aromatic; taste aromatic.

The epidermal cells have undulate walls except over the veins; non-glandular hairs uniseriate, 1- to 3-celled, curved and pointed, with thick walls and striated or papillose cuticle; glandular hairs with short stalks and either a 2- or 8-celled glandular head; stomata broadly elliptical with a pair of neighbor cells transverse to the pores, the cells frequently containing large sphere-crystals of a carbohydrate. The tracheæ are spiral or with simple and bordered pores and the fibers long, thin-walled, lignified, and with numerous pores. The pollen grains are somewhat spheroidal, about 35 microns in diameter and nearly smooth. Each epidermal cell usually has sphere crystals or an irregular crystalline mass of a carbohydrate.

Pennyroyal contains a volatile oil (about 3 per cent in the dried leaves and 1.3 per cent in the dried stems), a bitter principle and tannin. The volatile oil consists chiefly of the ketone pulegone, which gives the oil its peculiar properties; also the ketones hedeomol and menthone in small quantities; also formic, acetic and isoheptylic acids.

Hedeoma is a stimulant and a carminative; also an emmenagogue.

Oleum Hedeomæ or Pennyroyal Oil (U. S. P. 1831 to 1916) is a powerful but dangerous ecbolic and intestinal irritant. Its use in medicine has practically ceased.

European Pennyroyal, *Mentha Pulegium* Linné, a perennial herb found in moist sandy locations in central and southern Europe, yields a volatile oil similar to that from American Pennyroyal and has been substituted for it.

Wild Mint, *Mentha arvensis*, var. *canadensis* Linné, a perennial herb common in wet places in the United States, with ovate-oblong or lanceolate leaves, in the axils of which whorls or globular clusters of flowers arise. The plant has an odor of pennyroyal and yields 1.25 per cent of a volatile oil from which pulegone and thymol or carvacrol have been isolated.

Water Mint (*Mentha aquatica*), a plant found in wet places from New England to Delaware, yields about 0.34 per cent of a volatile oil having the odor of pennyroyal.

Oil of Russian Pennyroyal contains pulegone, but the botanical origin is not known.

Marjoram or Sweet Marjoram consists of the dried leaves and flowering tops of *Origanum majorana* (*Majorana hortensis*), an annual herb indigenous to southern Europe, northern Africa and western Asia and extensively cultivated as a pot or seasoning herb.

The leaves (see Fig. 299, *B*) are from 1 to 4 cm. in length and 0.6 to 20 mm. in width; both surfaces are grayish green, soft-downy, and glandular-hairy. The odor is distinctly aromatic, and the taste aromatic and somewhat pungent. It yields up to 1 per cent of a greenish volatile oil, 85 per cent of which is a mixture of borneol and camphor. It also contains some tannin and a large percentage of ash, mostly acid-soluble. The leaves of *Coriaria myrtifolia* (Fam.

Coriariaceæ) have been substituted for sweet marjoram. These are readily distinguished (see Fig. 299, *A*).

Marjoram is widely used as a condiment and occasionally as a mild stimulant and carminative.

Origanum or Wild Marjoram (U. S. P. 1820 to 1863; 1873 to 1894) is the herb of *Origanum vulgare* Linné, a perennial indigenous to Asia, Europe and northern Africa, and introduced into the United States. The plants prefer dry soil and are 0.5 to 1 meter high. The leaves are opposite, petiolate, roundish ovate, obtuse, entire, somewhat hairy below and pellucid-punctate. The flowers are terminal on the branches, forming a corymb-like panicle, have a purple, bell-shaped, 5-toothed calyx; a purplish 2-lipped corolla and 4 exserted stamens. The odor of the drug is strongly aromatic, marjoram-like; the taste warm, aromatic and bitter.

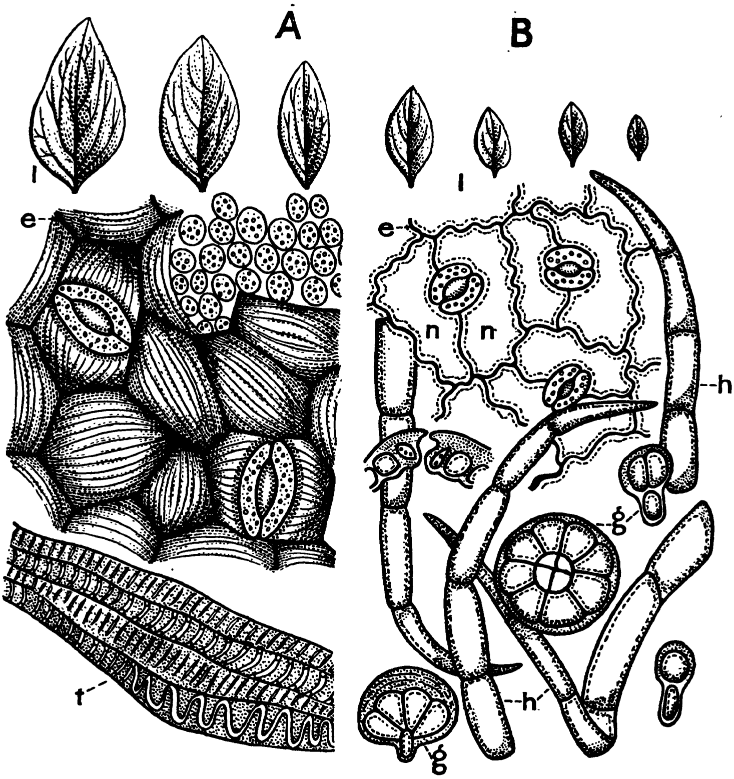


FIG. 299.—*A*, Coriaria: *l*, entire leaves; *e*, surface view of the lower epidermis showing two of the stomata with two neighbor cells which are situated parallel to the pore of the stoma; *t*, several of the trachea. The epidermal cells show a striated cuticle similar to the neighbor cells. *B*, Marjoram leaves: *l*, entire leaves; *e*, surface view of the lower epidermis showing three stomata, the neighbor cells (*n*) being at right angles to the pores of the stomata; *h*, uniseriate non-glandular hairs; *g*, typical 8-celled glandular hairs.

The herb contains volatile oil, about 2 per cent when recently dried, a little tannin and a bitter principle.

Oleum Origani or Origanum Oil (U. S. P. 1820 to 1863, 1873 to 1882) is pale yellow and limpid, becoming thicker and darker on exposure. It is strongly aromatic and pungent. It contains carvacrol and a stearoptene. It is often substituted with red oil of thyme.

It has been used as a counterirritant in toothache and neuralgia, in liniments, and internally in dysmenorrhea, colic, and as an emmenagogue. Dose, 0.3 cc.

Melissa, Balm or Lemon Balm (U. S. P. 1842 to 1905) is the dried leaves and tops of *Melissa officinalis* Linné. The plant is indigenous to southern Europe and western Asia and is naturalized and frequently cultivated in the United States and other countries. It attains a height of a meter. The leaves are up to 5 cm. long, broadly ovate, crenate-toothed. The inflorescence is axillary cymules of about 4 flowers each; calyx, bell-shaped, toothed, pubescent; corolla milk-white to pale purple, curved upward, the upper lip notched, the lower 3-lobed. The odor and taste of the drug are mildly aromatic, lemon-like. Balm is used as a pleasant tea. It is mildly diaphoretic.

Collinsonia or Stoneroot, is the dried rhizome and roots of *Collinsonia canadensis* Linné, a perennial herb, growing in moist woods throughout the central and eastern United States. The rhizomes with adhering roots are gathered in the fall and employed in either the fresh or dried condition.

The rhizome is horizontal, irregularly branched, from 3 to 15 cm. in length, and 1 to 2 cm. in thickness; externally light to dark yellowish brown, roughened from the bud-scales, short conical buds, root bases, stem bases and shallow stem-scars; very hard, tough; internally light yellowish, having a thin bark, a narrow layer of wood and a very large pith; odor slight; taste astringent, slightly pungent. The roots are filiform, dark brown, more or less curved and branching toward the ends.

The cork cells have yellowish brown walls; the pith parenchyma has thickened lignified walls; the small fibrovascular bundles are separated by broad medullary rays, the cells laden with starch. The numerous starch grains are mostly single, narrow cylindrical, ellipsoidal, pyriform, fusiform or reniform in shape and from 2 to 25 microns in length. The hardness of the root is due to the large amount of lignified tissue.

Collinsonia contains a saponin-like glucoside; a resin soluble in ether, partly soluble in alcohol; organic acids; tannic acid; mucilage and wax. Total ash about 3.25 per cent, with 0.55 per cent of acid-insoluble ash.

Collinsonia herb contains an acrid volatile oil.

Collinsonin is the resinous extract of Collinsonia prepared by pouring the alcoholic extract of the drug into 3 volumes of water, thus precipitating the resin.

Collinsonia is an astringent, a diuretic and a diaphoretic. It is used particularly in genito-urinary affections. Average dose of drug, 2 gm.; of collinsonin, 150 mg. The herb also has been used for similar effects, but is much milder.

SOLANACEÆ, OR NIGHTSHADE FAMILY

The plants are of varied form, most abundant in tropical regions, and the family comprises 85 genera and about 1800 species. The leaves are usually alternate; the flowers are mostly regular, excepting in *Hyoscyamus;* the anthers are connivent, the pollen sacs being apically or longitudinally dehiscent; and the fruits are superior berries or capsules. The plants are usually malodorous. They furnish a number of important economic products, including potato, tomato, egg plant and tobacco as well as a number of drugs.

The plants possess no special internal secretory tissues; bast fibers are usually wanting, except possibly in *Atropa Belladonna.* The medullary rays are generally narrow, and wood parencyhma is scantily developed. In *Atropa, Datura, Solanum* and *Scopolia,* an intraxylary phloem is frequently developed, in which sclerenchymatous fibers may occur. The walls of the pith cells are usually lignified in *Duboisia* and some other genera. Calcium oxalate is in the form of solitary crystals, rosettes or sphenoidal microcrystals. Both glandular and non-glandular hairs occur in a great variety of forms.

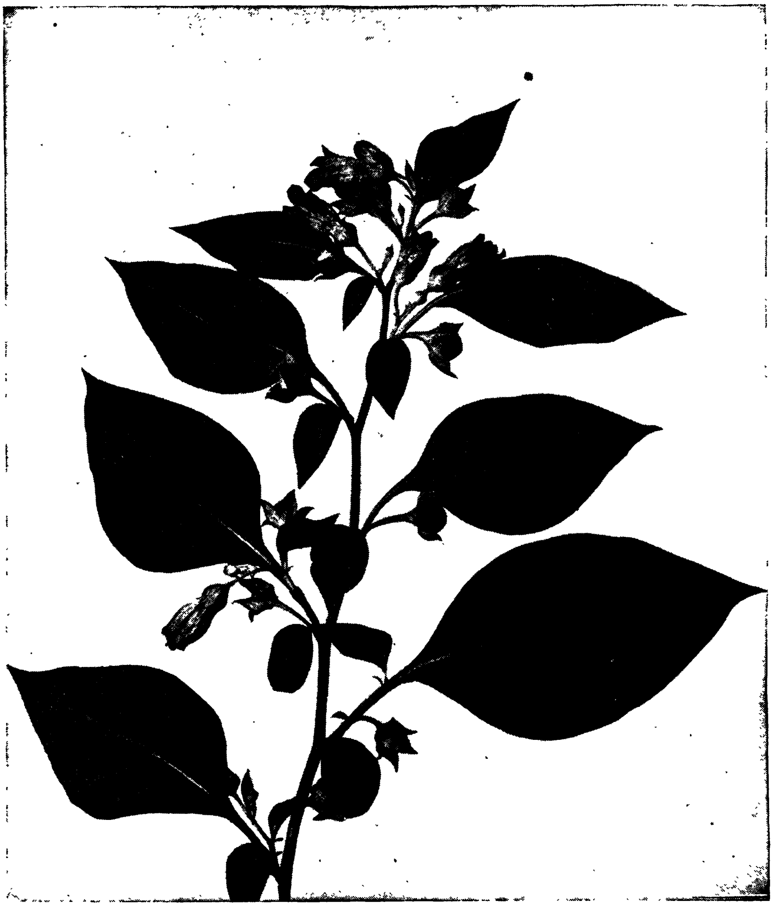


FIG. 300.—*Atropa belladonna* showing the alternate, petiolate, ovate, entire leaves, in the axils of which are the solitary fruits or flowers with large, leafy bracts.

BELLADONNA

Belladonna Leaf or Deadly Nightshade Leaf (U. S. P. 1820 to date) consists of the dried leaf and flowering or fruiting top with branches of *Atropa Belladonna* Linné, yielding not less than 0.3 per cent of the alkaloids of Belladonna Leaf.

Belladonna Root or Deadly Nightshade Root (U. S. P. 1863 to 1947; N. F. 1947 to date) is the dried root of *Atropa Belladonna* Linné, yielding not less than 0.45 per cent of the alkaloids of Belladonna Root.

Atropa is from *Atropos,* meaning inflexible, the name of the Greek Fate who cuts the thread of life, and probably alludes to the poisonous character of the drug. *Belladonna* is from the Italian, *bella,* beautiful, and *donna,* lady; the juice of the berry placed in the eyes causes dilation of the pupils, thus giving a striking appearance.

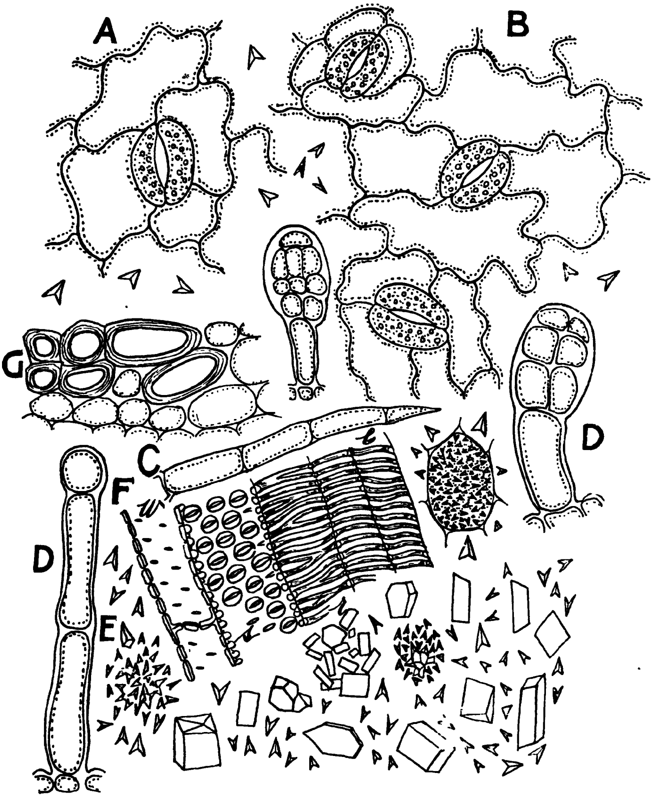


Fig. 301.—Belladonna Leaf: Of bifacial structure; epidermal cells with thin undulate walls, stomata and hairs (*A*) from the upper surface and (*B*) from the lower surface; a single palisade layer of short cells; a crystal layer of isodiametric parenchyma cells filled with sphenoidal microcrystals, the cells appearing grayish black; loose mesophyll with small bicollateral bundles. In the pericycle of the stem and in the internal phloem occur small groups of rather thin-walled slightly lignified bast; in the xylem of the stem (*F*) are tracheæ with annular, spiral, scalariform or reticulate markings and numerous thin-walled porous fibers. The non-glandular hairs (*C*) are few, uniseriate, 2- to 5-celled; the glandular hairs (*D*) may have a 2- to 3-celled stalk and 1-celled head, or a 1-celled stalk and many-celled head. The microcrystals are usually less than 5 microns in length and sphenoidal. Occasionally small starch grains and ellipsoidal pollen grains with 3 meridional furrows are noted.

The plant is a perennial herb, growing up to a meter in height, indigenous to central and southern Europe and Asia Minor, and is cultivated in sunny locations in England, Germany, India and the United States. Belladonna was probably known to the ancients, but the first authentic notice appears in 1504. The poisonous character of the plant was early known in the localities where it is indigenous. It was the subject of many treatises during the eighteenth century. Its mydriatic properties were first recorded in 1802 and its analgesic properties not until 1860. The leaves were used prior to the root, the latter not coming into general use until about 1860.

The stems are cut about half way down when the fruits begin to form and the alkaloids are most abundant. After rains or irrigation the plant produces a second crop of leaves and flowers, which is gathered in the fall. The roots are dug in the autumn, the larger ones being split to facilitate drying. Most of the herb crop is dried or partially dried and extracted with acidified water to obtain the alkaloids. A fine grade of leaf drug is obtained by hand picking the leaves and drying them rapidly at rather low temperatures and in the shade.

DESCRIPTION.—**Leaf Drug** (see Fig. 300). Usually in irregular, matted fragments. Stem hollow, cylindrical, flattened, longitudinally furrowed and wrinkled. Leaves 5 to 20 cm. in length, 4 to 12 cm. in breadth; upper surface dark green, glabrous; under surface grayish green, slightly pubescent on the veins, epidermis distinctly sinuate with whitish dots (crystal cells) visible with a lens; texture fragile. Flowers solitary, pedicel 1.5 to 2 cm. in length; calyx deeply 5-cleft about 1 cm. in length; corolla 5-parted, about 2 cm. in length, campanulate, yellowish purple; stamens 5, included; style somewhat exserted. Fruit, a superior berry, globular, dark green, 7 to 10 mm. in diameter, 2-locular, many-seeded. Seed campylotropous, somewhat reniform, flattened, light brown; testa finely pitted, with a curved embryo embedded in the endosperm. Odor distinct, somewhat tobacco-like; taste somewhat bitter and acrid.

Root Drug.—Cylindrical or tapering, somewhat branched, twisted, 0.5 to 4 cm. in thickness, occasionally split longitudinally; externally weak brown to moderate yellowish brown, or white where the soft periderm is abraded; fracture short and mealy, emitting a puff of dust consisting of starch grains and cell fragments; internally yellowish brown to pale yellow, slightly radiate; bark 0.5 to 2 mm. in thickness, not fibrous and adhering closely to the wood; cambium zone distinct. Odor characteristic, somewhat narcotic when moistened; taste sweetish, acrid.

STRUCTURE AND POWDER.—Leaf Drug: see Figure 301 and the U. S. Pharmacopœia. Root Drug: see Figures 302, 303, 304*B*, and the National Formulary.

CONSTITUENTS.—Belladonna contains hyoscyamine (in largest proportion); atropine, which appears to be derived from its isomer hyoscyamine and not to preëxist in the root; scopolamine (hyoscine); belladonnine and apoatropine, both of which may be decomposition products of hyoscyamine; a fluorescent principle, *b*-methyl-æsculetin; sphenoidal crystals of calcium oxalate; malic acid in the leaf; and considerable starch in the root. Total ash in leaf drug 9 to 16 per cent, in root drug about 5 per cent; acid-insoluble ash 0.3 to 0.7 per cent.

The yield of alkaloids averages about as follows: roots 0.6 per cent; stems 0.05 per cent; leaves 0.4 per cent; unripe berries 0.19 per cent; ripe berries 0.21 per cent; seeds 0.33 per cent.

STANDARDS.—Belladonna Leaf contains not more than 25 per cent of belladonna stems and not more than 3 per cent of stems, 10 mm. or more in diameter; it yields not more than 3 per cent of acid-insoluble ash.

Belladonna Root contains not more than 10 per cent of its stem bases and woody crowns and yields not more than 4 per cent of acid-insoluble ash. Roots that are shrunken, spongy, dark brown in color, or free from starch are to be rejected.

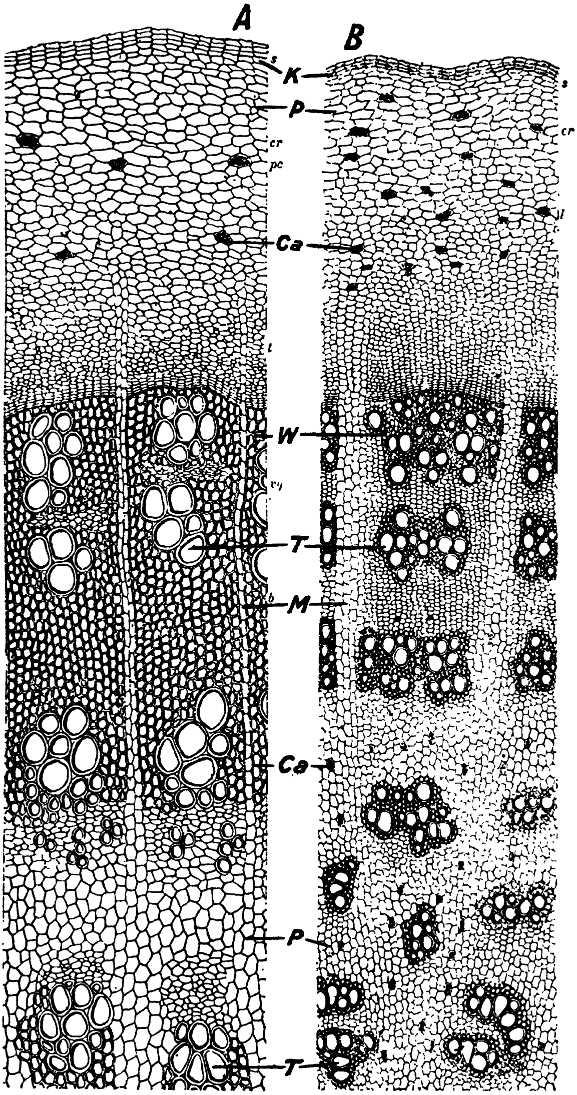


FIG. 302.—Belladonna Root: *A*, transverse section of an older root in which the xylem is completely developed. *B*, Transverse section of a lateral (younger) root in which the xylem portion is not so fully developed. The sections show cork (*k*) composed of a few layers of cells; a secondary cortex (*P*) composed of several layers of parenchyma, usually filled with starch and occasionally with microcrystals (*Ca*), the latter being relatively more numerous in younger roots; a phloem region devoid of bast fibers and traversed by medullary rays, the cells of the latter often containing starch or microcrystals of calcium oxalate; a conspicuous cambium zone; a broad xylem region composed of xylem wedges separated by medullary rays (*M*) the cells of the latter containing starch or microcrystals (*Ca*); the xylem wedges contain large reticulate tracheæ (*T*) in scattered groups separated by wood parenchyma (*P*) containing starch or microcrystals of calcium oxalate (*Ca*); the groups of tracheæ are associated with wood fibers (*W*) which are much more numerous in older roots; the medullary rays (*M*) are from 1 to 5 cells wide. (After Collin.)

Uses and Dose.—Belladonna stimulates the central nervous system, this effect being followed by depression. It decreases the flow of most secretions: saliva, milk, sweat. It has a sedative effect on the movements of the stomach and intestines, also upon the organs, the uterus, the bladder, etc. It dilates the pupil. It is therefore a stimulant, a narcotic, a sedative, an anodyne and a mydriatic. Average dose 60 mg. for leaf drug and 50 mg. for root drug.

Preparations of the leaf drug are more frequently used internally, and of the root drug externally in liniments, ointments and suppositories.

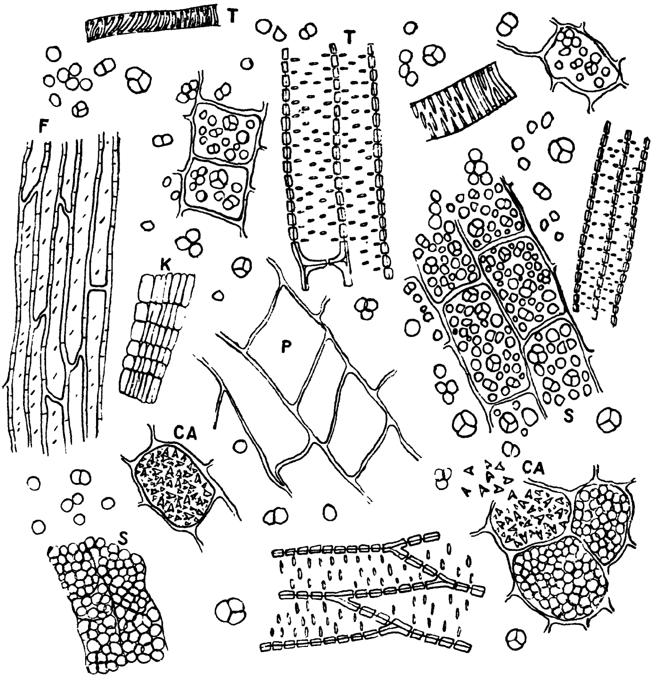


Fig. 303.—Powdered Belladonna Root. Ash gray to light brown; containing numerous simple or compound starch grains up to 30 microns in diameter, with a distinct, somewhat excentric hilum, showing polarizing bands which are usually more prominent in the larger grains; the starch is found separately or in starch-bearing parenchyma (*S*); microcrystals of calcium oxalate (*CA*) from 3 to 10 microns in length, often completely filling cells; wood fibers (*F*) with narrow oblique pores; tracheæ with annular markings or simple pores (*T*) and fragments of parenchyma tissue (*P*).

Adulterants.—Belladonna Leaf has been adulterated or substituted with Scopola leaves, Poke Root leaves, and *Solanum nigrum* leaves. Belladonna Root has been admixed with Poke Root, Scopola rhizome, Althea root, or Inula root. Poke Root (root or leaves) is detected by the presence of raphides of calcium oxalate and the diamond-shaped bordered pores on the tracheæ. Scopola (leaves or rhizome) is distinguished by the characteristic reticulo-scalariform markings on the tracheæ. Althea possesses numerous sclerenchymatous fibers while Inula has neither starch nor sphenoidal microcrystals.

Mandragora or European Mandrake is the root of *Mandragora officinarum.* The drug occurs in fusiform, somewhat bifurcated pieces and contains mandragorine (isomeric with atropine) and an alkaloid resembling hyoscyamine. Around this drug cluster many curious traditions. It was regarded with great veneration by the ancients, who recognized its narcotic properties.

Scopola (U. S. P. 1905 to 1916) is the dried rhizome of *Scopolia carniolica*, a perennial herb growing in the region of the eastern Alps, Carpathian Mountains and neighboring regions.

The rhizome is nearly cylindrical, somewhat tortuous, up to 12 cm. in length and 15 mm. in diameter; frequently sliced longitudinally; externally grayish brown, longitudinally furrowed, slightly annulate, with numerous circular stem-scars about 5 mm. in diameter; lower portion with root-scars and root remnants; fracture short, mealy; internally whitish or light grayish brown; bark 1 mm. or less in thickness, wood slightly radiate, pith rather large, horny; odor slight; taste starchy, sweetish, acrid.

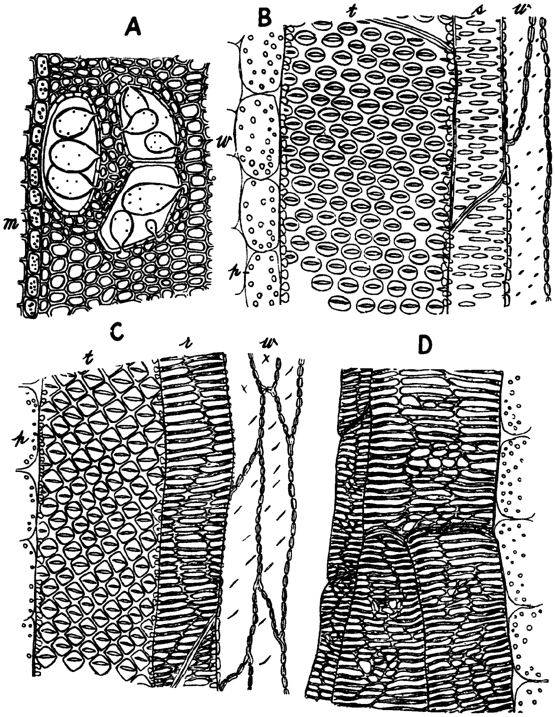


FIG. 304.—Different kinds of tracheæ. *A*, Transverse section of stem of grapevine (*Vitis vinifera*) showing three tracheæ from the older wood containing tyloses; *w*, wood fibers; *m*, medullary rays. The tyloses, or thyllen, are in the nature of ingrowths from the wood fibers and protrude through the adjoining pores, at the end of the season's growth, closing the cavities of the tracheæ. *B*, Longitudinal section of belladonna root showing a large trachea with bordered pores (*t*), a trachea with simple pores (*s*), wood fibers with oblique pores (*w*) and parenchyma (*p*) containing starch. *C*, Longitudinal section of phytolacca root showing a trachea with bordered pores (*t*), trachea with reticulate thickening (*r*), wood fibers (*w*) and parenchyma (*p*) containing starch. *D*, Longitudinal section of scopola rhizome showing the characteristic wide, reticulate tracheæ and portion of parenchyma containing starch.

The roots, attached or in pieces, are cylindrical, tapering, from 2 to 10 mm. in diameter, longitudinally wrinkled and marked by lenticular, whitish areas, resembling lenticels.

The structure of Scopola is illustrated in Figure 305.

Scopola contains about 0.6 per cent of total alkaloids, including atropine, hyoscyamine and scopolamine.

Scopola resembles belladonna root in therapeutic activity, although it is somewhat more narcotic because of the presence of scopolamine.

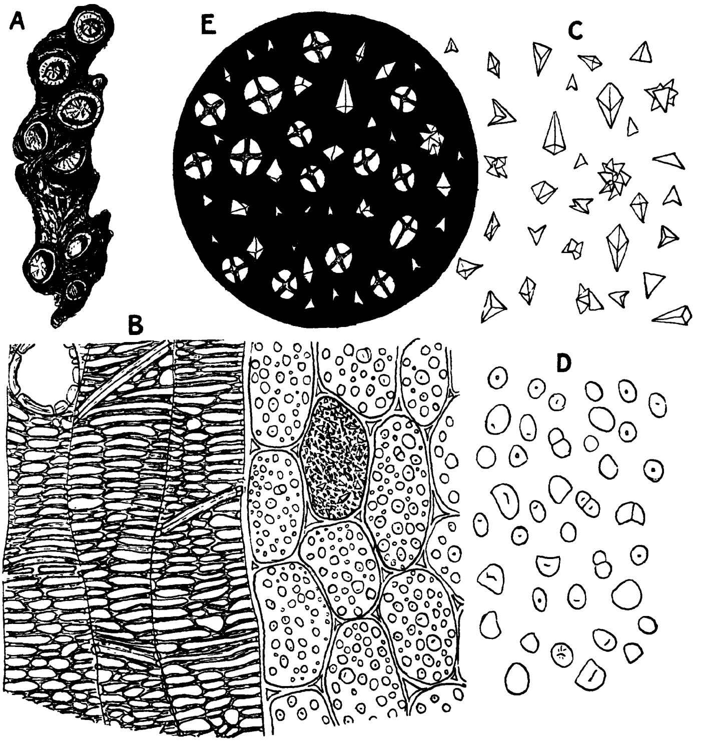


Fig. 305.—Scopola (*Scopolia carniolica*): *A*, rhizome showing prominent stem-scars. *B*, Longitudinal section showing reticulate tracheæ, parenchyma cells containing starch and sphenoidal microcrystals. *C*, Individual crystals which separate from sections or in the powder, the single crystals being from 5 to 10 microns in diameter and the aggregates being about 15 microns in diameter. *D*, Isolated starch grains, which are from 5 to 20 microns in diameter. *E*, Field showing starch grains and crystals under polarized light.

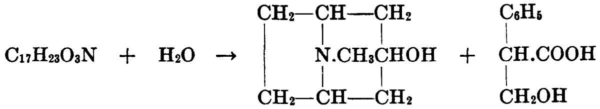
Scopola Leaf is the dried leaf of *Scopolia carniolica* and is used in medicine like Belladonna Leaf. The leaves are obovate, slightly acuminate and taper into the rather long petiole. The calyx lobes are relatively short and the capsular fruit (pyxis) is almost completely enclosed by the calyx tube. A few glandular hairs may be present. The tracheæ have annular, spiral or reticulate markings, and simple pores, but those with bordered pores do not occur. The sphenoidal crystals resemble those of belladonna. In glycerine preparations, spherite aggregates of carbohydrates are formed, especially in the calyx. The epidermal cells of the leaves are irregularly papillose, giving a tuberculate appearance in transverse section, and in surface view a deeply wrinkled or folded character to the walls. Bast fibers and wood fibers are not present, but there is a strongly developed layer of collenchymatous cells in the stem, the thickenings being more uniform and more marked than those in the similar cells of belladonna.

Japanese Belladonna is the rhizome of *Scopolia japonica,* growing in Japan, and closely related to *S. carniolica.* The drug resembles scopola and apparently contains the same principles. The rhizomes of six other species of *Scopolia* are also used.

THE SOLANACEOUS ALKALOIDS

The principal alkaloids of this group are hyoscyamine; its isomer atropine; scopolamine; and the anhydride of atropine, apoatropine and its isomer belladonnine. They are tropine derivatives, and are usually esters.

Hyoscyamine, $C_{17}H_{23}O_3N$, is the tropine ester of *l*-tropic acid, and is readily hydrolyzed by boiling in dilute acids or alkalis to form:



Tropine Tropic acid

Hyoscyamine occurs in colorless crystalline needles and is levorotatory. When it is extracted from the plants in which it occurs it usually is racemized during the process, being thus converted into the *dl*-compound, which is atropine.

Hyoscyamine Sulfate (U. S. P. 1882 to 1916) occurs as a white, fine, crystalline powder; it is very poisonous; 1 gm. is soluble in about 0.5 cc. of water, or 5 cc. of alcohol. Average dose, 0.5 mg.

Hyoscyamine Hydrobromide (U. S. P. 1894 to 1936) occurs as colorless crystals deliquescent in air, and very soluble in water, alcohol or chloroform. It is very poisonous. Average dose, 0.5 mg.

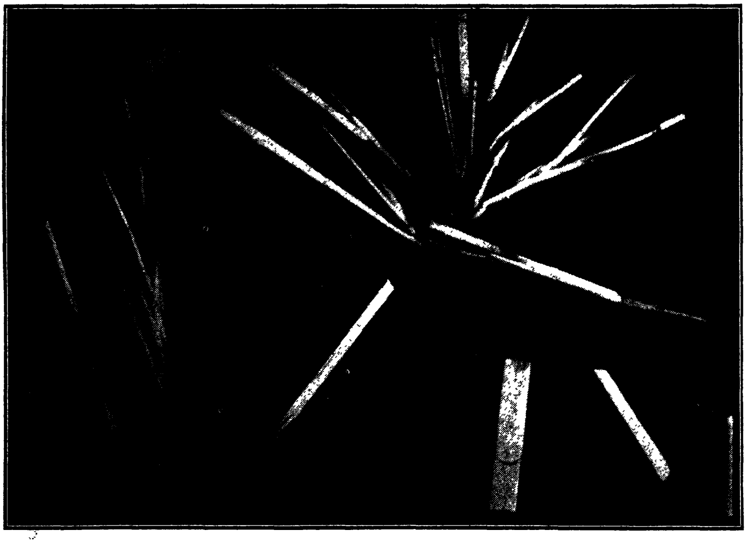


FIG. 306.—Atropine: Long orthorhombic prismatic crystals from an alcoholic solution.

Atropine, $C_{17}H_{23}O_3N$, (U. S. P. 1863 to date) is an alkaloid usually obtained from *Atropa Belladonna* Linné, from species of *Datura* or of

Hyoscyamus, or produced synthetically. It is extremely poisonous. It is considered to be non-preëxistent in the Solanaceous plants (except in traces) but to be formed from hyoscyamine during the process of extracting the drugs.

Atropine occurs in colorless, needle-like crystals or as a white, crystalline powder; it is optically inactive, but usually contains some levorotatory hyoscyamine, the limit of which produces an angular rotation not to exceed −0.70°. Consult the U. S. Pharmacopœia for its constants and tests of identification and purity. Average dose, 0.4 mg.

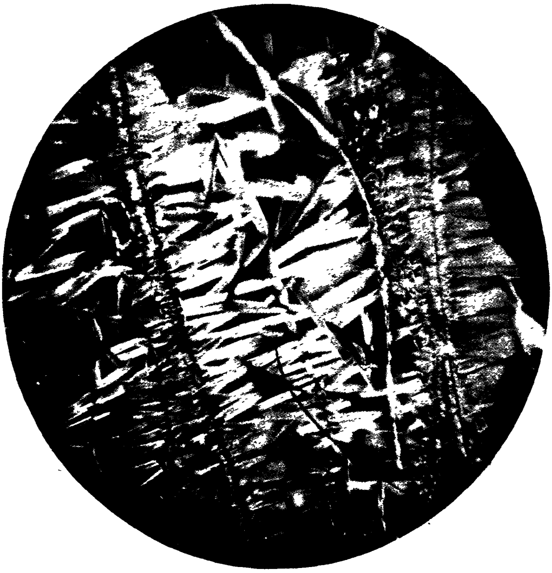


FIG. 307.—Scopolamine hydrobromide: Crystal aggregates from an alcoholic solution.

Atropine Sulfate (U. S. P. 1863 to date) occurs as colorless crystals or as a white crystalline powder. It is extremely poisonous. It effloresces in dry air, and is affected by light. Average dose, 0.5 mg.

Scopolamine or Hyoscine is an alkaloid obtained from plants of the *Solanaceæ.* It is particularly abundant in *Datura fastuosa* var. *alba* and in *Datura metel.* It is an ester which upon hydrolysis yields tropic acid and oscine or scopoline, a base resembling tropine.

It occurs as an almost colorless syrupy liquid from its chloroformic solution; as colorless crystals from its ether solution. It is levorotatory.

Scopolamine Hydrobromide or Hyoscine Hydrobromide (U. S. P. 1894 to date) ($C_{17}H_{21}O_4N.HBr.3H_2O$): Consult the U. S. Pharmacopœia for properties and tests. It is a powerful hypnotic which causes sleep very closely resembling natural sleep. Average dose, 0.5 mg.

Apoatropine or Atropamine, $C_{17}H_{21}O_2N$, occurs in the root of *Atropa Belladonna* in small quantity, and possibly in other Solanaceous plants. It can be prepared by heating atropine with nitric acid so as to cause the loss of one molecule of water. It occurs in colorless, bitter, optically inactive crystals. It is weakly mydriatic, stimulates the medulla and spinal cord and accelerates respiration.

Belladonnine is a yellow, amorphous, viscid mass giving no crystallizable salts. It probably contains apoatropine or an isomer of it. It belongs to the atropine group pharmacologically but is rarely used medicinally.

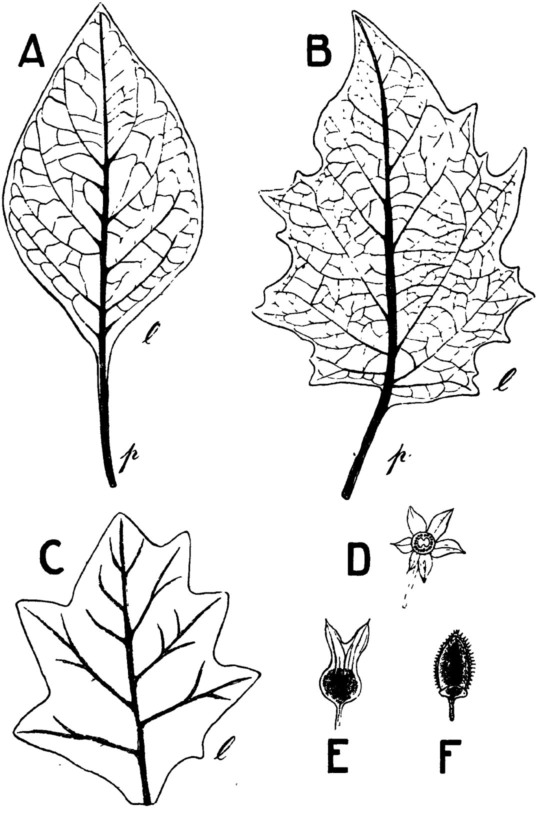


FIG. 308.—Leaves and fruits of Solanaceous drugs: *A*, *D*, Belladonna, the inferior berry, cut transversely, showing numerous seeds; *B*, *F*, Stramonium, the fruit being a spinose capsule; *C*, *E*, Hyoscyamus, the fruit being a pyxis, surmounted by the large calyx lobes.

Homatropine Hydrobromide (U. S. P. 1905 to date) ($C_{16}H_{21}O_3N.HBr$) is the hydrobromide of a synthetic alkaloid formed by the interaction between tropine and mandelic acid. It is extremely poisonous.

Consult the U. S. Pharmacopœia for properties and tests. The use of homatropine is confined largely to ophthalmic practice, it having the advantage over atropine in that the mydriasis is more rapidly produced, but less complete, and disappears more rapidly. Average dose, 0.5 mg.

Homatropine Methylbromide or Novatropine, $C_{16}H_{21}O_3N.CH_3Br$, (N. F. 1947 to date), when dried at 100° C. for three hours, contains not less than 3.7 and not more than 3.85 per cent of N. and not less than 21.3 per cent and not more than 21.9 per cent of Br.

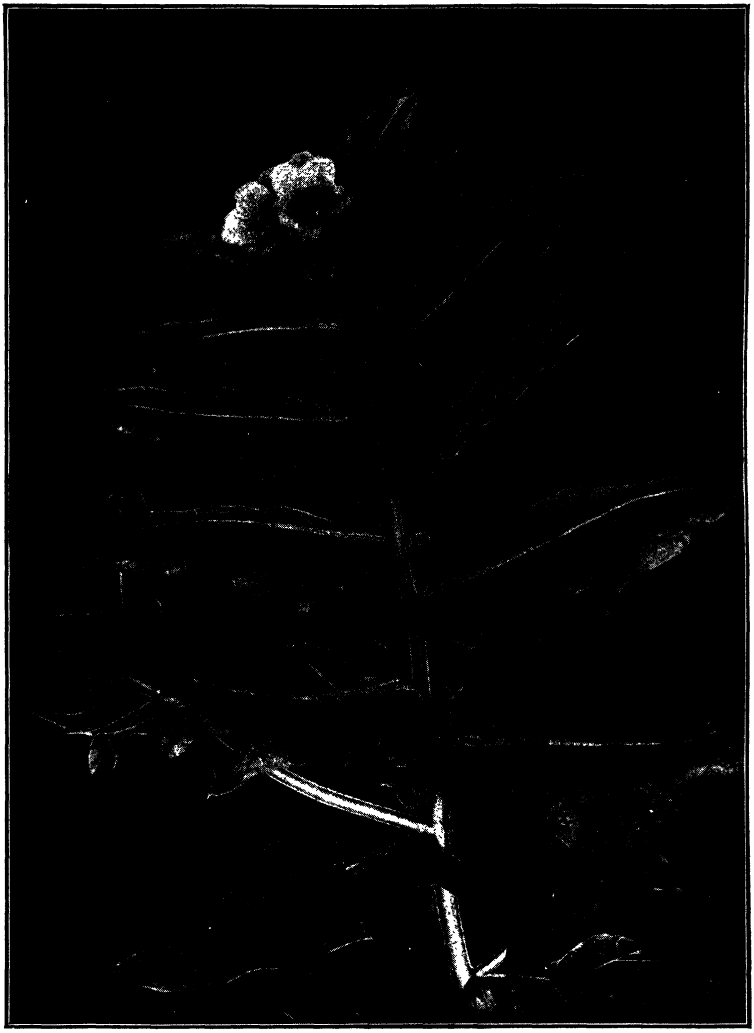


FIG. 309.—Flowering branch of *Hyoscyamus niger annuus*, showing sessile, acutely lobed leaves and two of the funnel-form flowers. (After Newcomb.)

It occurs as an odorless, white, crystalline powder with a bitter taste. It is extremely poisonous. It is used as a sedative, especially for gastro-intestinal spasms. It is less toxic than atropine. Average dose, 2.5 mg.

Eucatropine Hydrochloride, $C_{17}H_{25}O_3N.HCl$ (U. S. P. 1942 to date), when dried over sulfuric acid for four hours, contains not less than 86 per cent and not more than 89 per cent of eucatropine.

It occurs as a white, granular, odorless powder, readily soluble in water, alcohol and chloroform. Its solutions are neutral to litmus paper. It is extremely poisonous.

The drug produces prompt mydriasis, free from anesthetic action, pain, irritation, etc., and is used mostly for its mydriatic effect.

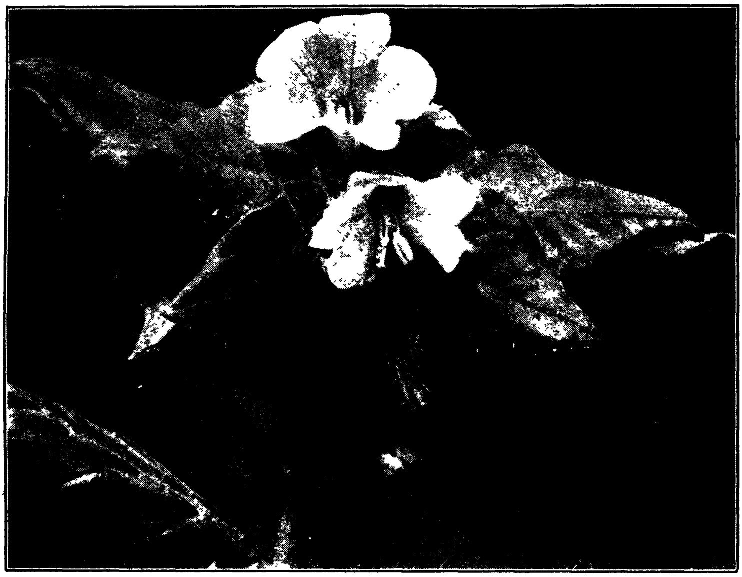


FIG. 310.—Flowers of *Hyoscyamus pallidus.* (After Newcomb.)

Pharmacologic Summary.—Atropine produces (1) complete paralysis of the peripheral distribution of the parasympathetic nerves (parasympathicolytic action), hence serves as a mydriatic; antisialagogue; antihydrotic; antidote to pilocarpine, muscarine and physostigmine; antispasmodic in colic, spastic constipation, etc.; for relaxation of the peripheral bloodvessels, hence a flushed skin and even erythema. (2) Atropine in small doses is a gentle stimulant to the respiratory and cardiac muscles. (3) Atropine on local applications causes a dullness or slight paralysis of the sensory nerves, hence used in liniments, ointments and suppositories it eases pain. (4) Atropine excites, then paralyzes certain cerebral and medullary centers, hence has a hypnotic, sedative and anesthetic effect.

To produce mydriasis, hyoscyamine is effective in one-half the concentration, scopolamine in one-fifth the concentration and homatropine in twice the concentration as that of atropine. On the other hand, the complete recovery from mydriasis with homatropine is but one-fifth as long as when atropine or scopolamine are used.

Hyoscyamine and scopolamine are used but little as mydriatics. They are definitely cerebral sedatives. Hyoscyamine is used to quiet excitability, especially in the insane; scopolamine is extensively used as a hypnotic in "twilight sleep," and has been suggested as a general anesthetic.

HYOSCYAMUS

Hyoscyamus or Henbane (U. S. P. 1820 to date) is the dried leaf, with or without the tops, of *Hyoscyamus niger* Linné and yielding not less than 0.040 per cent of the alkaloids of Hyoscyamus. *Hyoscyamus* is the ancient Greek and Latin name formed from two Greek words meaning hog and bean. The plant is said to be poisonous to swine.

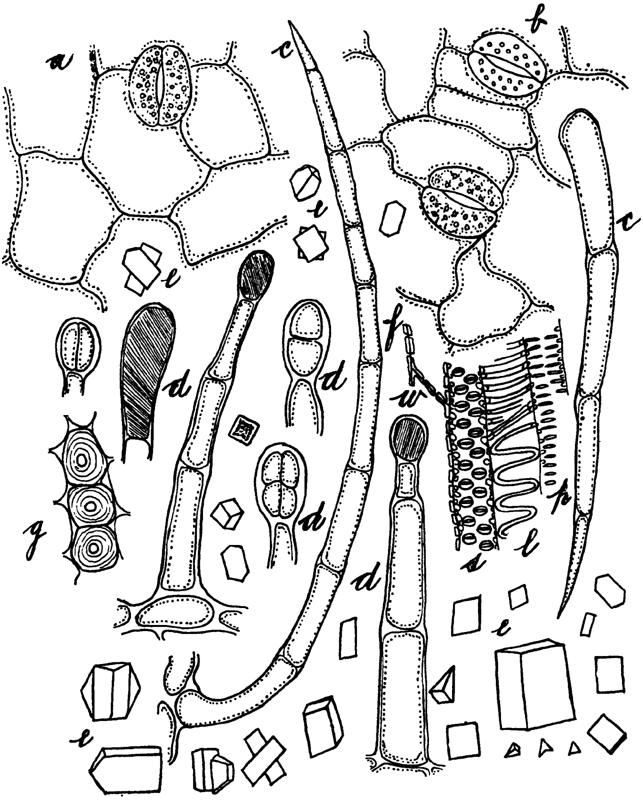


FIG. 311.—Hyoscyamus powder: grayish green to dark green; fragments of epidermis with nearly straight cell walls and stomata up to 35 microns long, (*a*) from upper surface of leaf, (*b*) from lower surface; (*c*) non-glandular hairs numerous uniseriate, 1- to 10-celled; glandular hairs (*d*) uniseriate, or with a 1- to 4-celled stalk and a 6- to 8- or many-celled head; calcium oxalate (*e*) mostly in monoclinic prisms up to 25 microns in length or rarely in rosettes or sphenoidal microcrystals; xylem fragments (*f*) showing spiral and dotted tracheæ and wood fibers with thin, porous, slightly lignified walls; fragments from midrib and stem showing strongly developed collenchyma, bast (*g*) and parenchyma; occasional pollen grains up to 40 microns in diameter, with 3 pores and 3 radiating furrows.

The plant is an annual or biennial herb (Fig. 309) indigenous to Europe, western Asia and northern Africa and cultivated in Russia, England and Germany, and to some extent in the United States and Canada. The biennial form is that most generally cultivated in England, the annual form being cultivated on the continent. The leaves should be gathered when the plant is in full flower and immediately be carefully dried. Although cultivated in the United States, the greater part of our supply comes from England and Germany. Dioscorides mentions the plant, and under the name of henbane it has been employed in European domestic medicine from the remotest times. Anglo-Saxon works on medicine in the eleventh century mention it as does also the Arabian Nights. After the Middle Ages the drug fell into disuse, but was reintroduced into regular medicine about 1760, largely through the efforts of Störck.

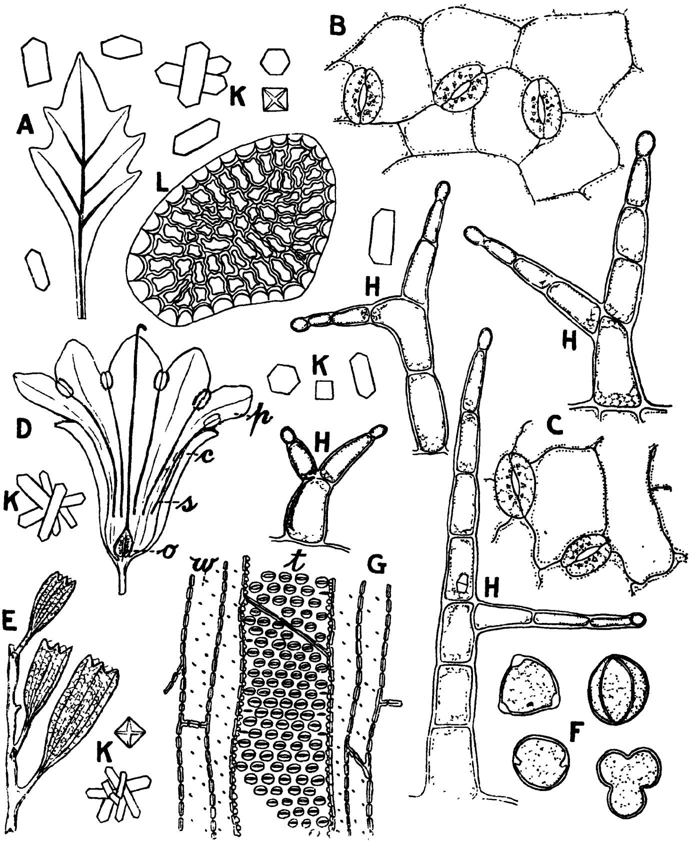


FIG. 312.—*Hyoscyamus muticus:* *A*, leaf. *B*, Portion of upper surface of leaf. *C*, Portion of lower surface. *D*, Section of flower showing calyx (*c*), lobed corolla (*p*), stamens inserted on corolla tube (*s*), ovary (*o*). *E*, Portion of stalk with fruits showing cylindrical calyx. *F*, Pollen grains in different views. *G*, Portion of xylem of stem showing tracheæ (*t*) with bordered pores, wood fibers (*w*) with oblique simple pores. *H*, Characteristic branching hairs found on the stem, leaves and calyx. *K*, Crystals of calcium oxalate. L, Seed with epidermal cells having wavy walls, those at the edge being seen in section and showing that the outer wall is not thickened.

DESCRIPTION.—Usually in irregular, matted masses. Stem hollow, cylindrical, flattened longitudinally furrowed and wrinkled, 2 to 7 mm. in diameter;

internodes 1 to 3.5 cm. in length. Leaves ovate or ovate-lanceolate, 5 to 10 cm. in length, 2 to 7 cm. in breadth; petiolate or sessile; apex acuminate, base amplexicaul, margin acutely 1- to 4-lobed; upper surface dark green and pubescent; under surface grayish green and strongly pubescent; texture fragile. Flowers solitary and with a pedicel about 4 mm. in length; calyx tubular, 5-toothed, pubescent; corolla 5-parted, the tube purplish, the limb yellowish, reticulate from purplish veins; stamens 5, declined, mostly exserted; stigma capitate. Fruit, a 2-locular pyxis. Seeds numerous, campylotropous, somewhat reniform, flattened, 1 mm. in length, light brown, finely pitted, with a curved embryo embedded in the endosperm; odor distinct; taste bitter and somewhat acrid.

STRUCTURE AND POWDER.—See Figure 311 and the U. S. Pharmacopœia. Hyoscyamus leaves resemble those of belladonna in structure, except that the crystal layer contains monoclinic prisms of calcium oxalate, the hairs are different as well as more abundant and the epidermal cells are but slightly undulate.

CONSTITUENTS.—The alkaloids hyoscyamine and scopolamine, 0.05 to 0.15 per cent, of which three-fourths is hyoscyamine; an odorous principle in the nature of a butyric ether or butyrin; a glucosidal bitter principle, hyospicrin; total ash, about 17.45 per cent; acid-insoluble ash about 3.25 per cent.

Hyoscyamus contains not more than 25 per cent of its stems, none of which is more than 7 mm. in diameter. It yields not more than 12 per cent of acid-insoluble ash.

USES AND DOSE.—Hyoscyamus is more narcotic than belladonna. It is an anodyne, a hypnotic and a narcotic. Average dose, 0.2 gm.

Henbane Seed or Hyoscyami Semen (U. S. P. 1831 to 1882) contains up to 0.16 per cent of alkaloids (mostly hyoscyamine) and has been extensively used for extracting these. Since Egyptian henbane has come into use as a rich source of the alkaloids, henbane seed has dropped out of use.

Henbane from *Hyoscyamus albus* is collected in continental Europe and contains from 0.20 to 0.56 per cent of alkaloids, principally hyoscyamine. It is used for the extraction of the alkaloids.

Egyptian Henbane, the dried leaves and flowering tops of *Hyoscyamus muticus,* yields from 0.5 to 1.34 per cent of total alkaloid, consisting largely of hyoscyamine. The plant is indigenous to and cultivated in Egypt, also in irrigated soils of southern California. The drug is used, perhaps entirely, for the extraction of its alkaloids.

Egyptian henbane displays many very characteristic branching, multicellular, non-glandular hairs (see Fig. 312). The admixture of henbane of high alkaloidal content with the official drug is dangerous. U. S. P. henbane should have a maximum limit of alkaloids, perhaps 0.1 per cent.

STRAMONIUM

Stramonium, Jimson Weed or Jamestown Weed (U. S. P. 1820 to date) consists of the dried leaf and flowering or fruiting tops of *Datura Stramonium* Linné or of *Datura Tatula* Linné, yielding not less than 0.25 per cent of the alkaloids of Stramonium. The name *Datura* is derived from the Sanskrit, *dhattura,* and the Arabic *tatura* or *tatula,* the native name; *stramonium* means stinkweed, from the French *stramoine.* The plant is an annual herb attaining the height of about 2 meters, indigenous to the region of the Caspian Sea, naturalized in waste places in Europe and North America and cultivated in France, Germany and Hungary. The leaves and tops are collected when the plant is in flower and are carefully dried and preserved, the chief portion of the commercial supply being obtained from plants cultivated in central Europe. The

Purple Stramonium (*Datura tatula*), which is naturalized in the United States from tropical America, is similar to *D. stramonium*, but the stems and flowers are purplish. The constituents in the two plants are alike. Stramonium was grown in England about the sixteenth century from seeds obtained from Constantinople. The early settlers near Jamestown, Va., used it as a "pot herb" with fatal results, thus establishing its common name. It forms one of our most important sources of atropine.

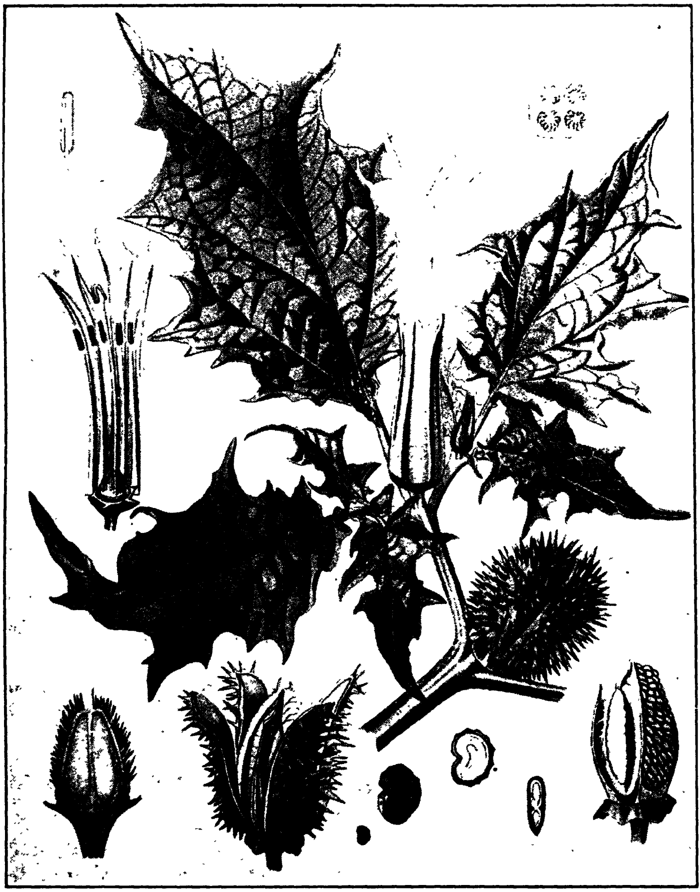


Fig. 313.—*Datura stramonium*. (After Köhler.)

Description.—Usually in irregular, matted masses. Stem cylindrical, flattened, longitudinally furrowed and wrinkled, 2 to 8 mm. in diameter. Leaves petiolate, ovate (Fig. 313), 6 to 20 cm. in length, apex acuminate; base unequal, margin irregularly sinuate-lobed, the lobes acute; surfaces grayish green to dusky olive green, glabrous except on lower surface of veins; texture fragile; flowers solitary; pedicel short; calyx 5-toothed, forming a collar at base of fruit; corolla white or purplish, plicate, funnel-shaped; stamens 5, epipetalous;

stigma bicarpellate. The immature fruit somewhat conical, 4-valved, covered with short, stiff emergences; seeds numerous. Odor distinct, heavy and narcotic; taste unpleasant, nauseous.

Structure and Powder.—See Figures 314 and 315.

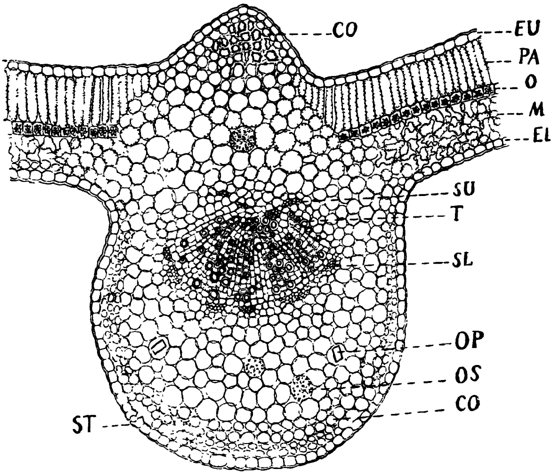


Fig. 314.—Transverse section of midrib of leaf of stramonium: *EU*, upper epidermis; *CO*, collenchyma; *PA*, palisade cells; *O*, layer of cells containing rosette aggregates of calcium oxalate; *M*, loose mesophyll; *EL*, lower epidermis; *OP*, prisms of calcium oxalate; *OS*, sphenoidal microcrystals of calcium oxalate; *ST*, stoma; *T*, tracheæ; *SU*, sieve on upper side of xylem; *SL*, sieve on lower side of xylem, this arrangement of sieve and tracheæ forming bicollateral fibrovascular bundles.

Constituents.—Hyoscyamine and atropine, the former being in excess; volatile oil; resin; total ash about 17 per cent, containing considerable potassium nitrate; acid-insoluble ash, about 0.2 per cent.

The amount of total alkaloids from the same plant has been reported as follows: roots, 0.2 per cent; stems, 0.02 per cent; leaves, 0.35 per cent; seeds, 0.40 per cent.

Uses and Dose.—Stramonium has an action much like that of belladonna. It is a narcotic, an anodyne and a mydriatic. Average dose, 75 mg.

Adulterant.—The drug from Spain and France has been entirely substituted by the leaves of *Xanthium macrocarpum* (Fam. *Compositæ*). The leaves are smaller, yellowish green and prickly hairy. There are several types of hairs, one being lignified.

Stramonii Semen or Stramonium Seed (U. S. P. 1820 to 1905) is the ripe seed of *Datura Stramonium* Linné. The ripening capsules are gathered and dried until the seed shake out. The seed are reniform, flattened, 3 to 4 mm. in length; externally bluish black, minutely reticulate; hard but easily cut lengthwise along the edge; internally whitish, the reserve layer occupying about one-half the seed, the embryo crook-shaped; odor slight, disagreeable when the drug is bruised; taste bitter.

The powder is brownish black or grayish black; epidermal cells with thick, somewhat mucilaginous outer walls, small lumina, and dark brown contents; subepidermal layer of thick-walled, nearly colorless cells with distinct, crescent-shaped lamellæ in the radial walls and reticulate pores. The cells of the endosperm contain considerable oil and aleurone grains, the latter having 1 or 2 crystalloids and a number of globoids.

Stramonium Seed contains about 25 per cent of fixed oil; proteins; about 0.4 per cent of alkaloids, consisting principally of hyoscyamine, together with a small proportion of atropine and scopolamine; ash 2 to 3 per cent.

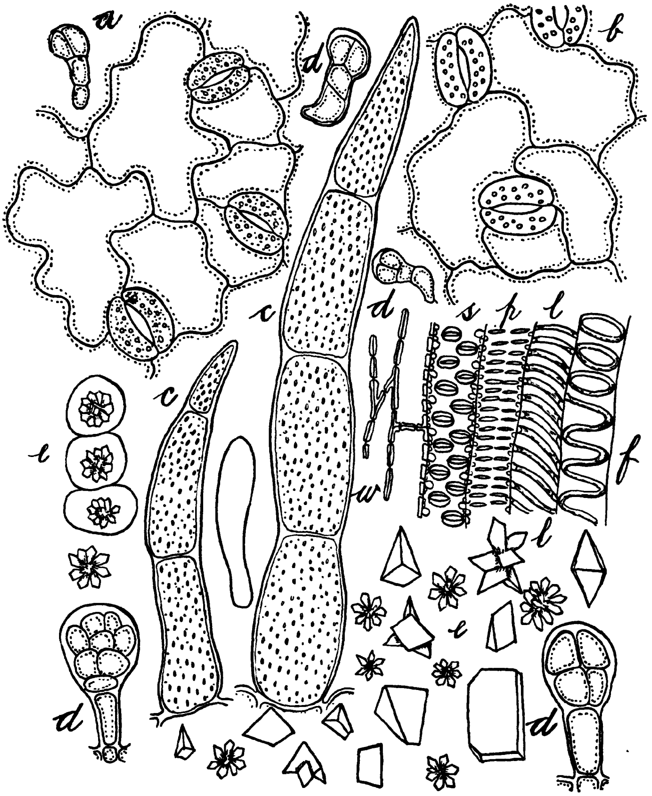


FIG. 315.—Stramonium powder: epidermal cells with sinuate walls, (*a*) from upper surface of leaf, (*b*) from lower surface; stomata elliptical, about 25 microns long, and having 3 to 5 neighbor cells; (*c*) non-glandular hairs, usually only few and on the younger leaves, uniseriate, 2- to 6-celled, up to 500 microns long and strongly papillose; glandular hairs few, 1- to 2-celled stalks and 2- to 4-celled heads; (*e*) calcium oxalate in rosettes, up to 25 microns in diameter, occasional prisms and microcrystals; (*f*) tracheal fragments showing spiral or porous markings; occasional fragments of wood fibers or wood parenchyma from the stem xylem.

Stramonii Radix or Stramonium Root (U. S. P. 1842 to 1863) is the root of *Datura Stramonium* Linné. The root is fleshy, much branched, with a knotty crown at the top. The thicker portions should be sliced and the drug carefully dried. It contains about 0.2 per cent of alkaloids, mostly atropine. It is often included with the herb, which, partially dried and chopped into pieces, is extracted in huge tanks with acidified water to obtain the alkaloids. In medicine belladonna root has superseded it.

Floripondio Datura, the leaves of *Datura arborea*, indigenous to Chile and Peru and cultivated for its handsome flowers, contain 0.44 per cent of solanaceous alkaloids; the leaves are used in medicine.

Duboisia is the dried leaves of *Duboisia myoporides*, a large shrub indigenous to Australia. The leaves are short-petiolate, 7 to 10 cm. in length, 1.5 to 2.5 cm.

in width, with an acute apex and base, and an entire or somewhat revolute margin; in the drug, usually in thin greenish brown fragments, with a distinct odor and a bitter taste. The drug contains hyoscyamine, scopolamine and pseudohyoscyamine; also a volatile alkaloid resembling piturine and nicotine.

The leaves of *Duboisia leichardtii,* of Australia, also contain a relatively large percentage of alkaloids.

Pituri or Australian Tobacco is the leaf of *Duboisia hopwoodi* and is used in Australia like tobacco. It contains 2.5 per cent of a liquid alkaloid, piturine, which has a pungent odor and taste and resembles nicotine.

Folia Nicotianæ or Leaf Tobacco (U. S. P. 1820 to 1905) consists of the cured and dried leaves of the Virginia tobacco plant, *Nicotiana tabacum. Nicotiana* was named after Jean Nicot, a French diplomat, who probably introduced tobacco into Europe; *tabacum,* or Spanish *tabaco* refers to the Indian name for the "pipe" or tube used for smoking it.

The plant is a tall annual herb indigenous to tropical America and widely cultivated. The stem is simple, giving rise to large, pubescent, ovate, entire, decurrent leaves, the veins of which are prominent and more or less hairy. The flowers are long, tubular, pink or reddish and occur in terminal spreading cymes. The leaves are hung in barns, and slowly cured and dried, using a little heat if the weather is cold or damp. Other species of *Nicotiana* are also cultivated, as *N. persica,* which yields Persian tobacco; and *N. rustica,* the source of Turkish tobacco.

The powder is greenish brown and shows 3- to 6-celled, non-glandular hairs, with a broad basal cell and not infrequently branching apical cells; glandular hairs of two kinds, either with a 1-celled stalk or a 3- to 5-celled stalk, the head in each case being rather small and with 8 to 9 cells; stomata large and with 2 or 3 neighbor cells; epidermal cells striated and somewhat granular on surface view; the cells of the mesophyll with a greenish brown content, some containing sphenoidal microcrystals.

Tobacco leaves contain from 0.6 to 9 per cent of the alkaloid nicotine; an aromatic principle, nicotianin, or tobacco camphor, to which the characteristic flavor is due and which is formed during the curing of the leaves. The dried leaves yield from 14 to 15 per cent of ash, consisting in large part of potassium nitrate.

Commercial tobacco has been adulterated with chestnut, cherry, rose, melilot, cabbage, chicory, beet and burdock leaves.

In the manufacture of plug tobacco various other substances are added; as licorice, cloves, anise, orris root, vanilla, deer's tongue leaves, tamarinds, prunes, etc.

Tobacco is a narcotic, a sedative, a diaphoretic and an emetic.

Nicotine, $C_{10}H_{14}N_2$, is an alkaloid obtained from cured tobacco (commercially from the stems, petioles, midribs, trimmings and dust from tobacco factories) in which it is present as citrate or maleate. The alkaloid is an oily, volatile liquid, colorless to yellow, slowly becoming brown on exposure to air; taste exceedingly acrid and pungent; odor of pyridine. It is very poisonous. It is a local irritant and paralyzant. Its salts (hydrochloride, salicylate and tartrate) occur as colorless crystals, readily soluble in water and considerably used in medicine. Nicotine salts, and largely a concentrated extract of tobacco containing about 40 per cent of nicotine, are used in sprays on fruit trees and other plants to destroy aphids or plant lice.

SOLANUM

Dulcamara or True Bittersweet (U. S. P. 1820 to 1905; N. F. 1916 to 1936) is the dried stem of *Solanum Dulcamara* Linné.

Solanum or Horse Nettle Berries (N. F. 1916 to 1936) consists of the air-dried ripe fruit of *Solanum carolinense* Linné.

Potato is the tuber of *Solanum tuberosum* Linné.

Eggplant is the nearly ripe fruit of *Solanum Melongena.*

Tomato is the fresh ripe fruit of *Lycopersicon esculentum* (*Solanum lycopersicum*).

Solanum Nigrum, or Black Nightshade is the flowering and fruiting herb of *Solanum nigrum* Linné.

Solanum is the ancient Latin name for Nightshade; *carolinense* refers to habitat; *Dulcamara* is from the Latin meaning sweet and bitter; *tuberosum* is Latin and refers to the enlargements or tubers on the slender rhizomes; *esculentum* refers to the edible nature of the fruit.

These plants all possess a bitter gluco-alkaloid identical with or similar to solanine. It occurs in the green parts of the potato plant, in the tubers (if green from the sunlight), and in the growing sprouts of the tubers. It is found in the leaves and fruits of Dulcamara, and in the green leaves and young green fruit of tomato and egg plant. These plants in the original wild form were quite poisonous.

Solanum dulcamara is a woody climber, indigenous to Europe and Asia, growing in moist thickets in the northern United States and southern Canada, and to some extent cultivated. The fruit is an ovoid or subglobular red berry sometimes eaten by children with fatal effects. The woody, 2- or 3-year-old twigs are gathered in the early spring or the late fall, cut into small pieces and dried.

Dulcamara is in short, hollow, cylindrical pieces, from 4 to 6 mm. in diameter; outer surface yellowish or greenish brown, longitudinally wrinkled or furrowed and frequently showing leaf-scars and a development of scaly cork; internally showing a thin, yellowish brown corky layer, a small, dark brown, somewhat lamellated cortex, a broad, yellowish, porous wood, and a large hollow pith; odor slight, distinct; taste of bark bitter, and of wood sweetish.

The powder is light yellowish brown, and contains fragments of lignified wood fibers having bordered pores, and associated with a few wide tracheæ possessing simple pores; occasional non-lignified bast fibers and fragments of yellowish brown cork; sphenoidal microcrystals from 3 to 7 microns in diameter; starch grains few, nearly spheroidal, from 5 to 12 microns in diameter; occasional long unicellular hairs having thick walls and a papillose cuticle.

Dulcamara contains a bitter glucosidal principle, dulcamarin, yielding upon hydrolysis glucose and dulcamaretin, the latter being tasteless; about 0.03 per cent of a glucoalkaloid, solanine, which forms prisms and is soluble in amyl alcohol, slightly soluble in hot alcohol, sparingly soluble in boiling water and upon hydrolysis yields dextrose and a crystalline alkaloid, solanidine. Total ash, having a greenish color, about 6 per cent, with about 0.7 per cent of acid-insoluble ash.

Dulcamara has been used as a sedative and hypnotic; also as a diaphoretic and a diuretic. It is also claimed to be of value as an alterative and resolvent in some skin diseases.

Solanum is from a perennial herb found in dry fields and waste places in the eastern and central United States. The fruit is a superior globose berry, collected when ripe, during the summer, and carefully dried.

Solanum is globular, much shriveled, from 7 to 20 mm. in diameter; externally yellowish brown or greenish brown, epicarp nearly smooth and shiny, and subtended by the 5-lobed hairy calyx; pericarp very thin and membranous, brittle; placentæ more or less fleshy and bearing numerous seeds; the latter are broadly elliptical or somewhat reniform, flattened, campylotropous, about 2 mm. in length, yellowish or dark brown and nearly smooth; odor slight, somewhat pepper-like; taste bitter and acrid.

The powder is brownish; the cells of the outer epidermis from 138 to 250 microns in length with very sinuous, yellowish, lignified walls about 15 microns in thickness; epicarp cells with thick yellowish walls and a yellowish amorphous content; portions of sarcocarp composed of thin-walled more or less collapsed cells, some containing nearly spheroidal starch grains, the latter up to 12 microns in diameter; narrow tracheæ with spiral or reticulate thickenings; occasional microcrystals.

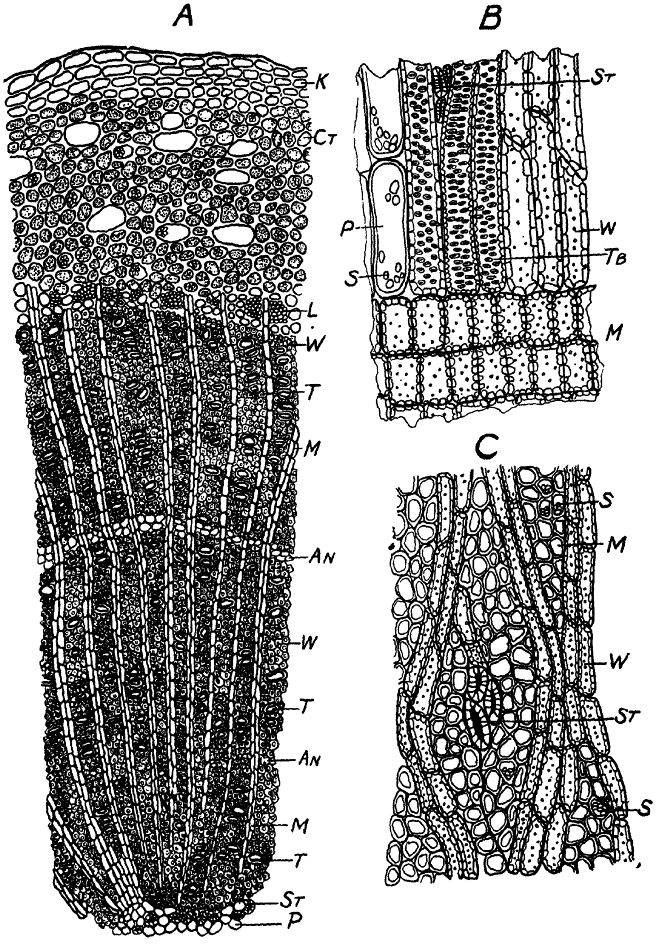


FIG. 316.—Manaca: *A*, transverse section of root: *K*, thin-walled cork which arises in the epidermal layer; *Ct*, cortex consisting mostly of starch-bearing parenchyma, and cells containing either rosettes of calcium oxalate or a yellowish brown amorphous content; the larger cells of which are mostly spheroidal in shape and usually lined with a thin layer of protoplasm; *L*, small strands of leptome; *W*, wood fibers; *M*, medullary rays consisting mostly of rectangular cells, having thick, porous walls; *An*, cells marking the rings of growth between the spring and fall wood as also of the cambium, usually filled with a yellowish brown, amorphous substance; *St*, stone cells, usually developed between the wood fibers and medullary rays. *B*, Longitudinal section showing tracheæ having bordered pores (*Tb*), parenchyma (*P*); starch grains (*S*) being from 4 to 15 microns in diameter; wood fibers (*W*); thick-walled medullary ray cells (*M*); stone cells (*St*). *C*, Tangential section showing medullary ray cells (*M*); starch (*S*); wood fibers (*W*); stone cells (*St*) (Drawing by Haase.)

Solanum contains an alkaloid, solanine, which crystallizes in orthorhombic prisms, that are insoluble in water and very soluble in chloroform and hot alcohol, and have an acrid and bitter taste, leaving a persistent tingling sensation on the tongue.

Solanum is an antispasmodic and a sedative.

Manaca (N. F. 1926 to 1936) is the dried root of *Brunfelsia hopeana*, a large shrub growing along streams in Brazil and other parts of tropical America. While all parts of the plants are used in Brazil, only the root has been introduced into general medicine.

The drug occurs in pieces, from 6 to 10 cm. in length and from 1 to 3 cm. in thickness; externally reddish brown, much wrinkled and with a scaly cork, which, with the thin cortex, is easily separable from the light yellowish wood; very tough; internally the bark is thin and reddish brown, the xylem large and very finely radiate; inodorous; taste sweetish and slightly bitter. The structure is shown in Figure 316.

Manaca contains manacine, a very poisonous alkaloid, resembling strychnine in its physiological actions. It also contains manaccine, and a resinous substance which is apparently identical with æsculetin.

Manaca is used as an alterative in rheumatism and syphilis.

CAPSICUM

Capsicum or Cayenne Pepper (U. S. P. 1820 to 1942; N. F. 1942 to date) is the dried fruit of *Capsicum frutescens* Linné, known in commerce as African Chillies, or of *Capsicum annuum* Linné var. *conoides* Irish, known in commerce as Tabasco Pepper, or of *Capsicum annuum* var. *longum* Sendt, known in commerce as Louisiana Long Pepper, or of a hybrid between the Honka variety of Japanese Capsicum and the Old Louisiana Sport Capsicum known in commerce as Louisiana Sport Pepper. Capsicum must be labeled to indicate which of the above varieties is contained in the package. Capsicum yields not less than 12 per cent of a non-volatile ether-soluble extractive.

Capsicum, from the Latin *capsa,* meaning a "box," refers to the partially hollow, box-like fruit; *frutescens,* Latin, refers to the shrubby character of the plant; and *annuum,* Latin, refers to the annual character of the plant.

Capsicum frutescens is a small spreading shrub, up to 1 meter high, indigenous to tropical America and cultivated in tropical localities in Africa, India, America and Japan. Apparently, the more tropical the climate, the more pungent the fruit. *Capsicum annuum* is an herbaceous, annual form cultivated in mildly temperate to semi-tropical localities in central and southern Europe, Mexico, United States and other countries, under the names of Garden Pepper, Paprika, Pimiento, Mexican Chillies, Tabasco Pepper, etc. All of these are less pungent than African Chillies, but are very desirable as condiments. The medicinal value of capsicum is as a rubefacient, which value depends upon its pungency. The U. S. Pharmacopœia recognized only the African Chillies as a medicinal agent for one hundred and twenty-two years; when a pungent controversy over the admission of *Capsicum annuum* to the monograph arose, the Revision Committee chose to delete the monograph, rather than to degrade it. The N. F. Committee admitted the monograph and the inferior Louisiana Peppers; now it can be expected that capsicum will soon disappear from the medicinal field, for when the official standards of a drug are degraded, that drug soon disappears from medicine.

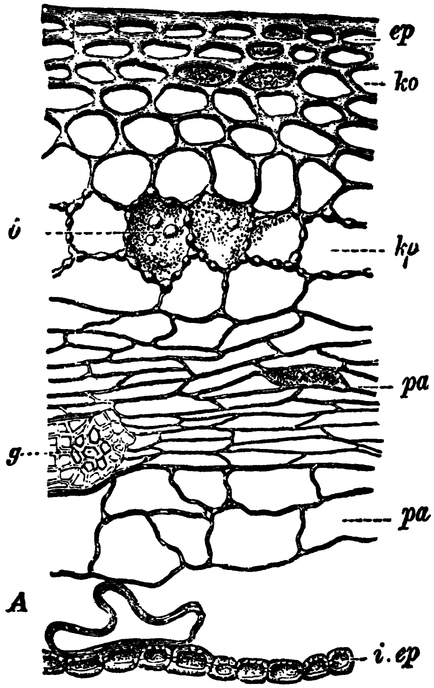


FIG. 317.—Garden pepper (*Capsicum annuum*): *A*, transverse section of pericarp showing epidermis (*ep*); hypodermis (*ko*); (*kp*) secretion cells having thick, porous suberized walls and containing oil (*o*) and resin; parenchyma (*pa*); fibrovascular bundle (*g*); inner epidermis (*i. ep*) composed of thick, lignified, porous cells.

African cayenne comes chiefly from the ports of Mombasa and Zanzibar in East Africa and Sierre Leone in West Africa, and is usually designated in the trade by the port named. Japanese chillies, usually exported from Kobe, are somewhat less pungent than African capsicum, but more pungent than Madras or Bombay chillies from British India. Of the 2 to 3 million pounds annually imported into the United States, about one-half comes from British India, one-third from Japan and one-sixth from Africa. Only the African should be used in medicine.

Capsicum was first referred to in 1494 by Chauca, a physician who accompanied Columbus on his second voyage to the West Indies. Plants were introduced into India by the Portuguese at an early date and later into Africa. Capsicum is official in nearly all the pharmacopœias of the world.

DESCRIPTION.—African chillies are oblong, conical, laterally compressed; from 10 to 25 mm. in length and from 4 to 8 mm. in diameter, rarely with a remnant of the calyx and a short pedicel; externally brownish red, glabrous, shiny, somewhat translucent, more or less shriveled; apex acute, base somewhat rounded; pericarp thin, brittle or somewhat coriaceous; inner surface with two or three distinct longitudinal ridges, longitudinally striate, 2- or 3-locular, dissepiments thin, united below; seeds 6 to 20, campylotropous, irregularly circular or obovate, flattened, pointed, about 2 to 4 mm. in diameter, 0.5 mm. in thickness, edge slightly thickened, embryo curved, embedded in the endosperm; odor distinct, sternutatory; taste extremely pungent.

Structure.—See Figures 317, 318, 319, and the National Formulary.

Powder.—Yellowish brown to brownish red; outer epidermis of pericarp mostly of quadrangular cells up to 80 microns long arranged in regular rows (Fig. 318), with thickened and cutinized outer and radial walls, the surface of the cuticle finely striated and the radial walls somewhat wavy and very slightly beaded; inner epidermis of pericarp of elongated cells, some of them very thin-walled, others in large oval areas with thickened, beaded, lignified walls; seed epidermal cells up to 250 microns in length, with very wavy, contorted, lignified walls; collenchymatous cells with suberized walls and containing yellowish-red oil globules and irregular masses of chromoplastids; small, thin-walled parenchyma cells from the endosperm containing aleurone grains and fixed oil; small, spheroidal starch grains, single or compound, from unripe fruits, rare; glandular hairs with 1- to 3-celled stalks and multicellular heads from the calyx, rather rare.

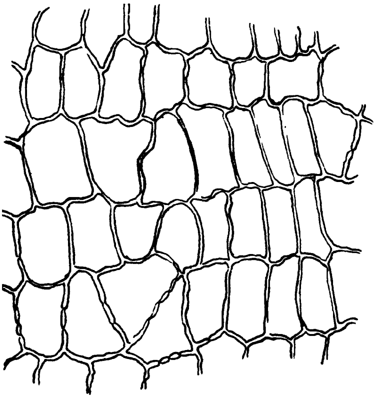


Fig. 318.—Cayenne Pepper (*Capsicum frutescens*). Surface section of the epidermis showing the rectangular-shaped, rather thin and but slightly beaded walls and the regular rows of the cells. (Drawing by E. N. Gathercoal.)

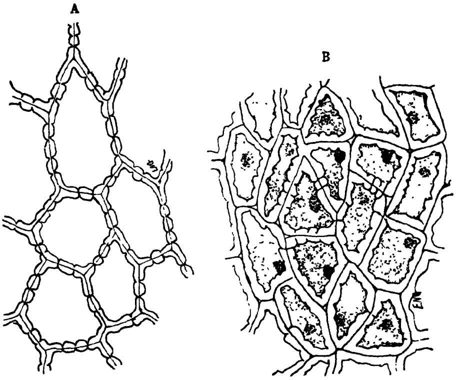
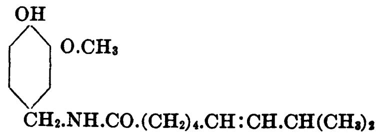


Fig. 319.—Garden Pepper (*Capsicum annuum*). Surface sections of *A*, epidermis, and *B*, hypodermis, showing the thickened beaded walls and non-rectangular shape of the cells. (Drawings by E. N. Gathercoal.)

Tabasco Peppers are about twice the size, and the Louisiana Peppers up to ten times the size of African Capsicum. The outer epidermis of the pericarp of these peppers consists of irregular (not quadrangular) cells with thickened and strongly beaded, lignified, radial walls; also a hypodermis of elongated cells with thickened, strongly beaded radial walls of cellulose or cuticularized cellulose. These features readily distinguish these peppers, in whole or powdered form, from genuine African capsicum (see Figs. 317 and 319).

Constituents.—Capsicum contains capsaicin (about 0.02 per cent), an extremely pungent principle in the dissepiments of the fruit. Capsaicin is a phenol having the formula:



Capsaicin imparts a distinctly pungent taste to water, even when diluted to 1 part in 11 million parts of water. Its pungency is not destroyed by alkalis as is that of gingerol, but is destroyed by oxidizing agents (potassium dichromate or potassium permanganate). Capsicum also contains a volatile alkaloid resembling coniine; a volatile oil with an odor of parsley; resin; a small quantity of starch; a fixed oil, consisting of olein, palmitin and stearin; and yields 4 to 6 per cent of total ash with about 0.45 per cent of acid-insoluble ash. The red coloring principle of the pericarp is very slightly soluble in alcohol, but soluble in ether, petroleum ether, carbon disulfide and chloroform.

Hungarian paprika is particularly rich in ascorbic acid (vitamin C).

STANDARDS.—Capsicum contains not more than 3 per cent of its stems and calyxes, and not more than 1 per cent of other foreign organic matter, yields not less than 12 per cent of non-volatile, ether-soluble extractive and not more than 1.25 per cent of acid-insoluble ash.

Thoroughly mix 1 gm. of powdered capsicum with 50 cc. of alcohol and allow to macerate for twenty-four hours; dilute 0.1 cc. of the clear supernatant liquid with 140 cc. of distilled water containing 10 per cent of sucrose; 5 cc. of this dilution swallowed slowly will produce a distinct sensation of the pungency of capsicum in the throat of at least 2 out of 3 individuals. This dilution is equivalent to 1 part of capsicum in 70,000 parts of sweetened water. Japanese capsicum so diluted 1 in 50,000 or Indian capsicum 1 in 40,000 will give about the same degree of pungency. Paprika and other capsicum fruits permit less dilution even down to 1 in 5000.

USES AND DOSE.—Capsicum is used as a rubefacient; it is also a stimulant and a condiment. Average dose, 60 mg.

ADULTERANTS.—Powdered capsicum is sometimes admixed with about 1 per cent of a fixed oil to improve its appearance, and such powders are likely to contain in addition some of the commercial starches or by-products obtained in the manufacture of cereal products.

Less pungent varieties are occasionally admixed with the drug. These may be readily detected by the character of the epicarp. Capsicum is itself used to enhance the pungency of other spice drugs, notably black pepper, ginger and mustard.

ALLIED DRUGS.—**Japanese Capsicum** is conical, from 15 to 44 mm. long, bright red externally, with usually more than 20 seeds and very rarely with an adherent calyx and peduncle.

Indian or Madras Capsicum is of two types: a narrow conical variety, 15 to 45 mm. long, 5 to 12 mm. wide, shrunken and flattened; and a short, conical variety, known as Madras Cherries, 15 to 30 mm. long, up to 20 mm. in diameter and sometimes nearly globular. The external color is frequently yellowish brown or reddish brown because these fruits were gathered before being fully ripened.

Paprika, Hungarian Paprika or Turkish Paprika, is a large-fruited pepper obtained from varieties of *Capsicum annuum*. Its origin is somewhat obscure. It apparently is indigenous to America and can be traced from its introduction into Spain thence to Greece, Turkey and Hungary. Paprika is recognized by the German Pharmacopœia. The fruits when fresh are 5 to 10 cm. in length, 5 to 7 cm. in diameter, more or less inflated, externally of a bright red color; the pericarp is 2 to 3 mm. in thickness, enclosing a large cavity, which has 1 or 2 dissepiments at the base, and contains numerous flattened seeds about 3 to 5 mm. in diameter.

Rosenpaprika, Rozsapaprika, or Rose Paprika, is Hungarian paprika prepared by grinding specially selected pods of paprika, from which the placentæ, stalks, and stems have been removed. It contains no more seeds than the normal pods, not more than 18 per cent of non-volatile ether extract, not more than 23 per cent of crude fiber, not more than 6 per cent of total ash, nor more than 0.4 per cent of ash insoluble in hydrochloric acid. It possesses a beautiful red color and a pungent, savory taste.

Königspaprika, or King's Paprika, is Hungarian paprika prepared by grinding whole pods of paprika without selection and includes the seeds and stems naturally occurring with the pods. It contains not more than 18 per cent of non-volatile ether extract, not more than 23 per cent of crude fiber, not more than 6.5 per cent of total ash, nor more than 0.4 per cent of ash insoluble in hydrochloric acid.

Pimenton, Pimiento, or Spanish Paprika, is paprika having the characteristics of that grown in Spain. It contains not more than 18 per cent of non-volatile ether extract, not more than 21 per cent of crude fiber, not more than 8.5 per cent of total ash, nor more than 1 per cent of ash insoluble in hydrochloric acid. The succulent pericarp is much used for stuffing olives, while the dry pod is ground as a spice. The pods are nearly spheroidal, from 2.5 to 4 cm. in length and 4 to 6 cm. in diameter, of a bright red color, and with no perceptible pungency. The pericarps have a sweet, acid taste and a peculiar odor. The seeds have a slightly bitter, bland taste, with a slight odor. The placentæ are dark red in color and have a taste similar to the pericarp.

SCROPHULARIACEÆ, OR FIGWORT FAMILY

This is a large family, represented by 205 genera and nearly 2600 species of herbs, shrubs or trees. The plants are characterized by having gamopetalous corollas, which may be nearly regular but are usually 2-lipped, the stamens being frequently didynamous and the fruits usually capsular. Among the anatomical characteristics the following may be mentioned: neither a subepidermal collenchyma nor a sclerenchymatous ring in the pericycle are developed; calcium oxalate is secreted in the form of small prisms, octahedra or acicular crystals. The non-glandular hairs are: (*a*) unicellular; (*b*) uniseriate; (*c*) unicellular, having cystoliths; and (*d*) multicellular, or branching, as in *Verbascum* and *Paulownia.* The glandular hairs are (*a*) those having a unicellular stalk and a unicellular secreting head; (*b*) those having a 2- or more-celled glandular head; (*c*) peltate-glandular. The mesophyll of the leaves contain not infrequently crystals of carotin, or protein substances. In *Scrophularia,* idioblasts containing tannin extend from the epidermal layers to the fibrovascular bundles.

DIGITALIS

Digitalis or Foxglove (U. S. P. 1820 to date) is the dried leaf of *Digitalis purpurea* Linné. Its potency is such that, when assayed as directed, 0.1 gm. shall be equivalent to not less than 1 U. S. P. Digitalis Unit or 0.1 gm. of the U. S. P. Digitalis Reference Standard.

Powdered Digitalis or Digitalis Pulverata (U. S. P. 1936 to date) is Digitalis dried at a temperature not exceeding 60° C. to a moisture content of not more than 5 per cent, reduced to a fine powder and adjusted, if necessary, so that 0.1 gm. of it shall be equivalent to 1 U. S. P. Digitalis Unit (a variation of not more than 20 per cent from standard in the assay results is permitted). When Digitalis is prescribed, Powdered Digitalis is to be dispensed.

Digitalis is from the Latin *digitus*, meaning a finger, and refers to the finger-shaped corolla; it was so named by Tragus in 1539; *purpurea* is Latin and refers to the purple color of the flower. The plant is a biennial herb, probably indigenous to central and southern Europe and naturalized in various parts of Europe and in northern and western United States and Canada. The leaves are collected from both the first and second year plants, usually from July to September. They may average higher in glucosides just before the expansion of the flower, and sunlight favors production of glucosides which at night appear to be partially hydrolyzed. Collections should be made in the afternoon,

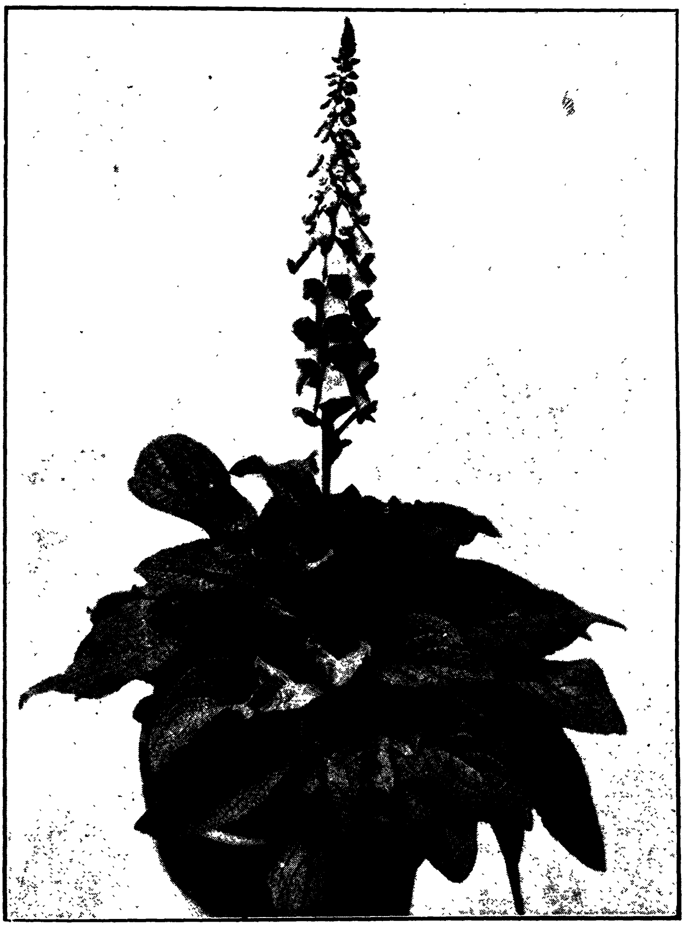


FIG. 320.—Specimen plant of *Digitalis purpurea*, grown in the Medicinal Plant Garden, University of Minnesota. (Photo by Newcomb.)

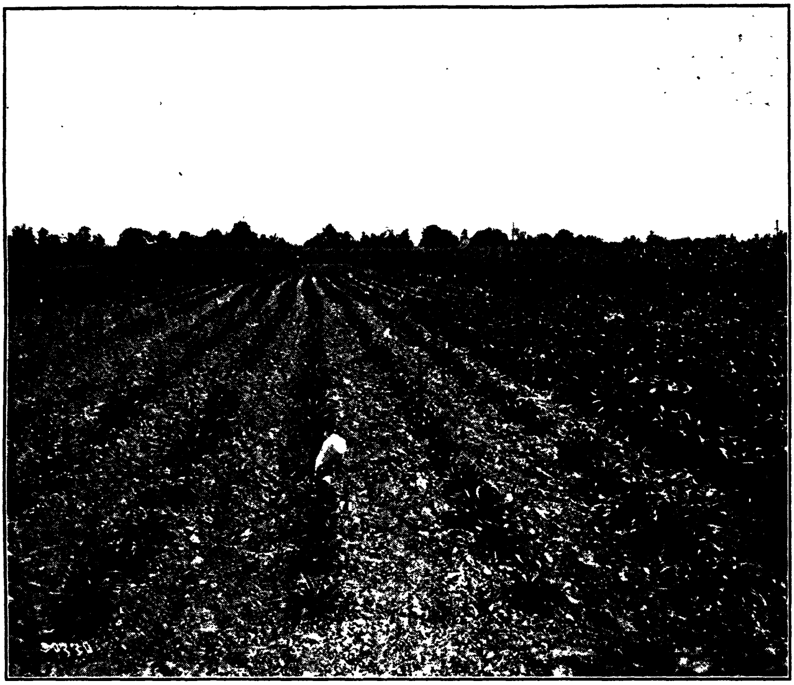


FIG. 321.—Cultivation of Digitalis: A general view of the Experimental Farm of Eli Lilly & Co., showing the testing and breeding of various species and varieties of *Digitalis*. (After Miller.)

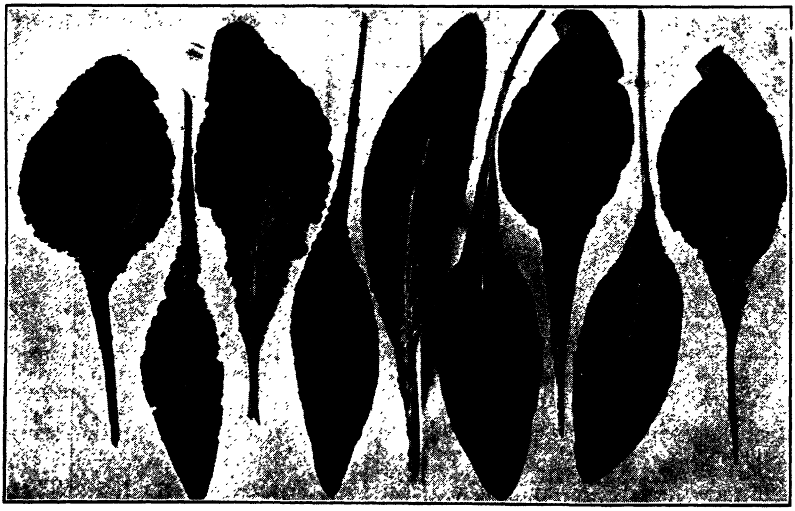


FIG. 322.—*Digitalis purpurea:* Leaf variations in different plants. It will be noted that the leaves vary in shape, margins and character of the petioles. There is also considerable difference in the color of the leaves and their surfaces. These variations seem too great and diversified to be explained as individual variabilities. (After Miller.)

be dried rapidly and thoroughly at a temperature of 55° to 60° C. in a drying room, then stored in water-proof air-tight containers. Some digitalis is imported from England and central Europe, but the larger supply comes from plants cultivated in Pennsylvania, the Pacific Northwest and Minnesota. Digitalis seems to have been used externally by the Welsh. Parkinson recommended it in 1640, but its internal use was not in vogue until its recommendation by Withering in 1776. It has been official in most pharmacopœias since the eighteenth century and in all editions of the U. S. Pharmacopœia.

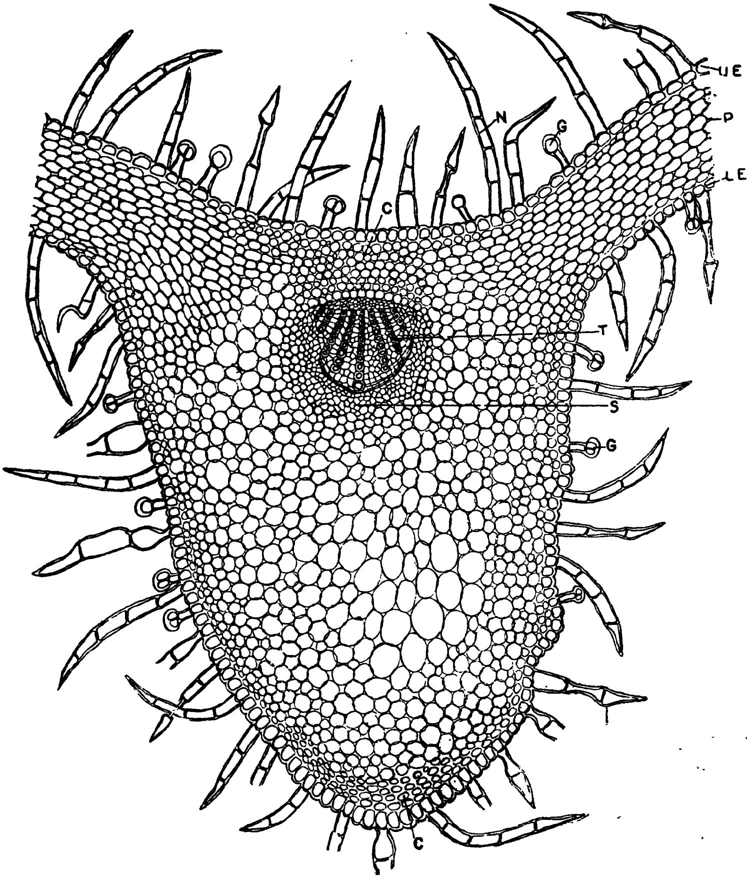


FIG. 323.—Transverse section of Digitalis leaf, through one of the veins: *UE*, upper epidermis; *P*, chlorenchyma (mesophyll), containing chloroplastids; *LE*, lower epidermis; *G*, glandular hairs; *N*, non-glandular hairs; *C*, collenchyma; *T*, tracheæ or vessels; *S*, leptome or sieve.

DESCRIPTION.—Usually more or less crumpled and broken into fragments; lamina ovate or ovate-lanceolate, 10 to 35 cm. in length, 5 to 11 cm. in breadth;

apex obtuse or rounded; base tapering into a winged petiole; margin dentate or crenate; upper surface dark green, minutely hairy, somewhat wrinkled, with a single waterpore near the summit of each tooth; under surface grayish green; midrib grayish brown, prominent; venation distinctly reticulate; densely pubescent on the veins and reticulations; petiole up to one-third the length of the lamina or, especially in the upper leaves, nearly wanting; fragile; odor distinct, peculiar and characteristic when moistened; taste very bitter.

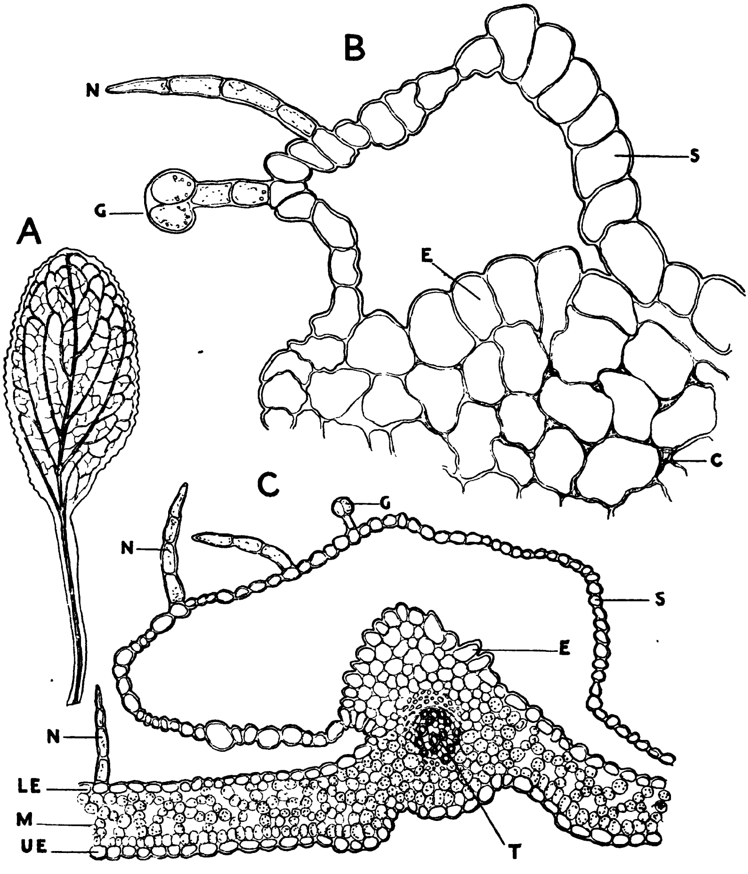


FIG. 324.—Digitalis: *A*, a typical leaf showing the winged or laminate petiole and the veins of the first order which diverge from the mid-vein at very acute angles; *B*, transverse section of portion of leaf showing the separated or additional epidermal layer (*S*); epidermal layer (*E*); glandular hair (*G*); non-glandular hair (*N*); collenchyma (*C*). *C*, Transverse section near one of the veins showing considerable of the separated or extra epidermal layer (*S*); with two non-glandular hairs (*N*) and glandular hair (*G*); epidermal layer (*E*); lower epidermis (*LE*); chlorophyl layer (*M*); upper epidermis (*UE*); tracheæ or vessels (*T*).

STRUCTURE AND POWDER.—See Figures 323, 324, 325 and the U. S. Pharmacopœia.

CONSTITUENTS.—Several glucosides, among which digitoxin, from 0.2 to 0.3 per cent is the most important; digitalin (crystalline), gitalin (crystalline), and probably others, as well as the saponin digitonin; a volatile oil containing a stearopten, digitalosmin, which has the odor of digitalis and a nauseous, acrid taste; a volatile principle, antirrhinic acid, somewhat resembling valeric acid; digitalic acid, separating in white needles; two coloring principles, one red and the other yellow, resembling chrysophan, a glucoside found in rhubarb; an oxydase ferment which occurs in the recently dried leaves; and a small quantity of tannic acid. Total ash, 7 to 12 per cent, with about 0.5 per cent of acid-insoluble ash.

Digitalis Semina or Digitalis Seed (U. S. P. 1831 to 1842) is the dried seed of *Digitalis purpurea* Linné.

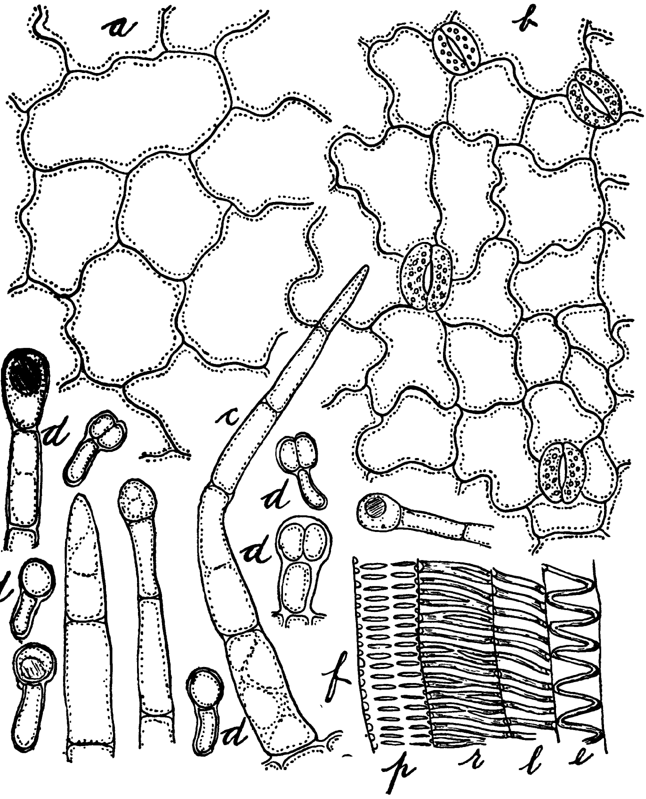


FIG. 325.—Powdered Digitalis: non-glandular hairs (*c*), uniseriate, of 2 to 8 (usually 2 to 5) cells, from 145 to 500 microns in length, often curved or crooked, some of the cells frequently being collapsed; glandular hairs (*d*), few, small, with a 1- to 2-celled stalk and 1- or 2-celled glandular head; numerous irregular fragments of lamina showing epidermal cells (*a* and *b*) having undulate walls and scattered stomata or occasional water-pores; fragments of veins (*f*), with annulate (*l*), spiral (*e*), or reticulate (*p*) tracheæ; calcium oxalate absent.

Digitalis seed are 1 mm. or less in diameter, yellowish brown to dark brown, more or less plano-convex, and tuberculate. Digitalis seed contain glucosides and a saponin somewhat like those of digitalis leaf. Schmeideberg's *digitalinum verum* in white crystals was from the seed. The seed may not contain digitoxin. Preparations of the seed have not replaced those of the leaves in medicine.

The Glycosides of Digitalis

The active constituents of Digitalis are frequently referred to as the cardiac glycosides because they are characterized by the highly specific and powerful action which they exert upon the cardiac muscles. In the natural state the glycosides are associated with saponins, also glycosidic substances, which affect the solubility of the cardiac principles, but are inert therapeutically. Though the pharmacological activity of the glycoside resides in the aglycone portion of the molecule, the sugars when combined with the aglycones increase both the potency and toxicity of the active principle. In addition the sugars affect certain physical properties of this chemical combination, such as water solubility and diffusion through semi-permeable membranes and therapeutically they determine the persistence of the cardiac action. The aglycones can be desugared by acid or enzymatic hydrolysis. Chemically, the aglycones are related to the bile acids and sterols, have an empirical formula as $C_{23}H_{34}O_{(4-8)}$. The basic structure is a cyclopentenophenanthrene nucleus to which is attached a lactone ring. The unsaturated lactone ring is indispensable whereby a reduction of the double bond reduces its toxicity and if there is a complete disappearance of the double bonds the compound is therapeutically inactive. In addition to the effects of substitution of hydroxyl groups for hydrogen, the stereochemical configuration markedly influences the physiological activity of these compounds. The various digitalis glycosides have different solubilities in aqueous and organic solvents. They are usually soluble

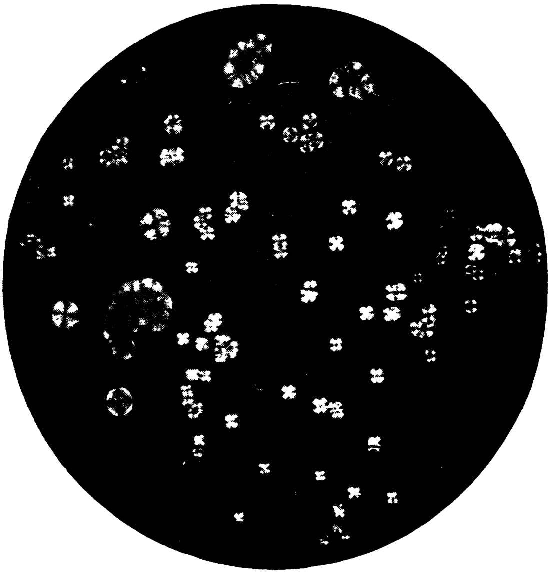


FIG. 326.—Digitoxin: sphero-crystals from an alcoholic solution.

in water or aqueous alcohol and almost insoluble in the usual fat solvents with the exception of chloroform and ethyl acetate. They can be obtained from the drug by exhaustive extraction with methyl alcohol.

Constituents of Digitalis Purpurea.—The important constituents are purpurea glycosides A and B, and gitalin. There are also present digitonin, hydrolytic enzymes and an oxidase. Purpurea glycosides A and B, frequently referred to as deacetylanatosides A and B or deacetyldigilanid A and B, occur in the natural state as precursors or "natural glycosides." Upon enzymatic hydrolysis purpurea glycoside A and B each yield one molecule of glucose and the glycosides digitoxin and gitoxin respectively. Upon further hydrolysis with an acid, digitoxin, gitoxin and gitalin yield the same sugar, but different aglycones, namely digitoxigenin, gitoxigenin and gitaligenin respectively. Digitoxin and gitoxin each yield three molecules of digitoxose and gitalin only two molecules.

Digitoxin (U. S. P. 1947 to date) is a well-defined, colorless, odorless, crystalline, bitter substance, insoluble in water, but nevertheless passing into solution in appreciable quantity when Digitalis leaves are infused in that menstruum. It is more or less soluble in alcohol and colored green with hydrochloric acid. It may be identified by Keller's reaction, which consists in dissolving it in glacial acetic acid, adding a drop of ferric chloride solution, and then, gently, sulfuric acid to form a layer below the acetic acid. A brownish green band is first formed after which the acetic acid layer becomes greenish blue and then indigo blue, while the sulfuric acid becomes brownish red. Digitoxin is the most toxic of the active constituents of the leaves, and is accumulative in action.

Gitalin is one of the three main glycosidal fractions of *Digitalis purpurea*. It was first obtained from a cold water extract of digitalis leaves by Kraft in 1912. He gave it the name "Gitalin"; it was subsequently introduced into clinical practice under the name of "Verodigen." It is not to be confused with the chemically pure glycoside gitalin, which has an empirical formula of $C_{35}H_{56}O_{12}$ and occurs as white rosettes melting at 245° C. The commercial product gitalin, recognized by the N. N. R., is an amorphous substance and probably not a chemical individual. It is a yellowish-white amorphous powder, which is very soluble in chloroform and alcohol and in about 800 parts of cold water. In the dry state it is quite stable retaining its action without any change in potency or deterioration over periods as long as two years. Pharmacological and clinical reports claim for it all the effects produced by whole digitalis preparations, with more accurately controllable conditions of absorption and therapeutic action.

Digitonin resembles quillajasaponin in its physiological action, and on hydrolysis yields dextrose, galactose and digitogenin. It is crystalline, soluble in water, somewhat soluble in alcohol and remains colorless on treatment with hydrochloric acid, but a sulfuric acid solution becomes garnet-red in color on boiling for some time. Digitonin, when anhydrous, occurs as an amorphous body, while with $5H_2O$ it is a crystalline, chemically uniform body.

Constituents of Digitalis Lanata.—Stoll isolated from the leaves of *Digitalis lanata* three chemically pure glycosides, known as lanatoside A, lanatoside B, lanatoside C, also known as digilanid A, digilanid B, and digilanid C, respectively. They all contain an acetyl group which on alkaline hydrolysis can be split off, giving rise to deacetyldigilanids A, B and C. Stoll also demonstrated that an enzyme, lanatosidase present in the leaves, splits one molecule of glucose from each of the compounds, leaving the acetyl glycosides. Upon alkaline hydrolysis these compounds lose the acetyl group, yielding the corresponding glycosides. These glycosides are digitoxin from lanatoside A, gitoxin from lanatoside B, and digoxin from lanatoside C. On enzymatic hydrolysis of the lanatosides, both the glucose molecule and the acetyl group are removed and the respective glycosides are liberated. Two of these glycosides, digitoxin and gitoxin, found in *Digitalis purpurea* are identical with the corresponding glycosides derived from lanatoside A and B, respectively. Digitoxin and gitoxin from both sources on further acid hydrolysis each yields three molecules of the same sugar, digitoxose and the corresponding aglycones, digitoxigenin and gitoxigenin, respectively. At the same time no counterpart of the glycoside digoxin, obtained from lanatoside C, can be found in *Digitalis purpurea* while gitalin in the latter cannot be found in *Digitalis lanata.* Stoll demonstrated that the glycosides digitoxin and gitoxin are actually degradation products of the compounds as they exist in the natural state. These natural glycosides in *Digitalis purpurea* are identical with those in *Digitalis lanata* except that they lack the acetyl group. The yield of pure genuine glycosides from *Digitalis purpurea* is very much smaller than that from *Digitalis lanata.* The components in both kinds of digitalis plant vary in different specimens within one and the same species and in different localities. The proportion of the three components in the average digilanid mixture has been found to be about 46 per cent of lanatoside A, 17 per cent of lanatoside B, and 37 per cent of lanatoside C.

Lanatoside C (U. S. P. 1947 to date) is a pure substance possessing a characteristic crystalline form with a melting point of 245° to 248 °C. It is easily soluble in methyl or ethyl alcohol. Although only slightly soluble in water, this solubility suffices for its therapeutic use. The empiric formula is $C_{49}H_{76}O_{20}$. On enzymatic and alkaline hydrolysis the glucose and acetyl radicles are liberated, leaving the glycoside digoxin. Further acid hydrolysis splits off three molecules of digitoxose leaving the aglycone, digoxigenin. Lanatoside C is a stable, easily absorbed, and promptly effective preparation which can serve as a potent therapeutic agent.

Digoxin (U. S. P. 1947 to date) is derived by hydrolytic cleavage from the natural glycoside lanatoside C of *Digitalis lanata,* or *Digitalis orientalis* and is formed by a chemical combination of a pentose sugar, digitoxose, with the cardioactive aglycone, digoxigenin. It is a stable crystalline substance. The drug is promptly and fairly completely absorbed and is cumulative.

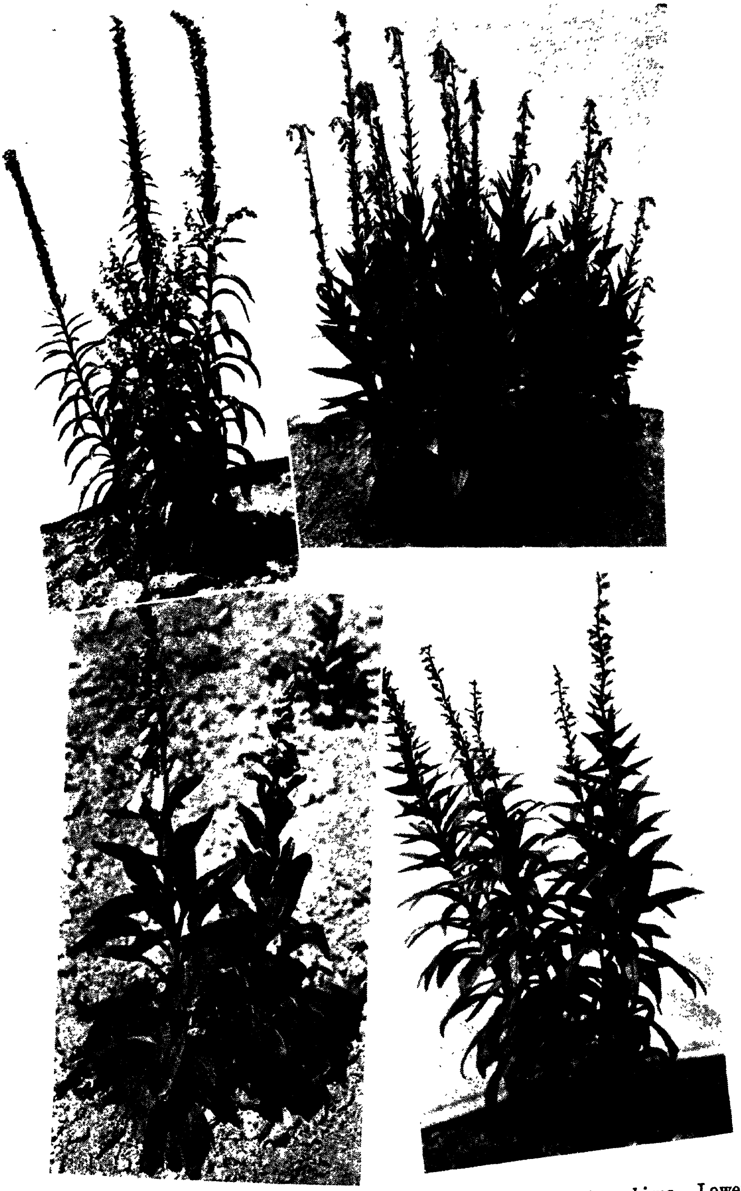


FIG. 327.—Upper left: *Digitalis lanata.* Upper right: *Digitalis ambigua.* Lower left: *Digitalis purpurea.* Lower right: *Digitalis siberica.* (The Glenolden Experimental Gardens.)

Uses and Dose.—Digitalis increases the contractility and improves the tone of the cardiac muscle; both reactions resulting in a slower but much stronger heart beat; also digitalis stimulates the vagus center, which tends to diminish the cardiac tone and excitability, thus counteracting the stimulating and strengthening effect of the peripheral action. This explains the need of careful dosage to be determined experimentally for each patient. The effective therapeutic dose may be as high as 70 per cent of the toxic dose. Because of its stimulant action on the heart and the improved circulation, the drug tends to improve renal secretion (diuretic), relieve edemas, and aid the cardiac muscle to compensate for mechanical defects or structural lesions. The finely powdered leaves or the tincture are still considered the most desirable forms for digitalis medication.

Adulterants.—In times past digitalis leaf has been adulterated or substituted with several kinds of hairy leaves, such as those of: *Piper angustifolium* (Fam. *Piperaceæ*), *Salvia Sclarea* (Fam. *Labiatæ*), *Verbascum phlomoides* or *D. thapsus* (Fam. *Scrophulariaceæ*), *Inula conyza* (Fam. *Compositæ*); also from several non-official *Digitalis* species, as *D. monstrosa.* Since standards have become more stringent, practically all adulteration of digitalis, except with inferior quality of the true drug, has ceased.

Allied Drugs.—**Digitalis grandiflora,** growing abundantly in Switzerland, produces leaf drug said to be as effective as the official Digitalis.

Digitalis Lutea or Straw Foxglove is the dried leaves of *Digitalis lutea;* it has been used in place of the official Digitalis and appears to be almost identical in activity, though perhaps less irritant.

Digitalis Ferruginea or Rusty Foxglove is the dried leaves of *Digitalis ferruginea* and is nearly twice as toxic as the official drug; the activity, however, is similar.

Digitalis Lanata or Grecian Foxglove is the dried leaves of *Digitalis lanata,* a plant indigenous to southern and central Europe and cultivated in southern California.

Digitalis Thapsi or Spanish Digitalis is the dried leaves, usually with the stems, flowers and capsules of *Digitalis thapsi.*

LEPTANDRA

Leptandra, Culver's Root or Veronica (U. S. P. 1820 to 1831, 1863 to 1916; N. F. 1916 to date) consists of the dried rhizome and roots of *Veronicastrum virginicum* (Linné) Farwell (*Veronica virginica* Linné). The name *Leptandra* is from two Greek words meaning slender and man, referring to the slender stamens; *Veronica* refers to St. Veronica.

The plant is a perennial herb growing in meadows and moist woods of the eastern and central United States and Canada. The rhizome and roots are collected in autumn from plants of the second year's growth. When fresh the drug has an almond-like odor and a bitter, nauseous taste, which it loses in a measure on drying. It may be kept indefinitely. Most of the commercial supply comes from Virginia and the Carolinas. The plant is often cultivated for its beautiful flowers. The plant was widely known to the American Indians; it was employed by them, as well as the white settlers, as a violent purgative. Its use was confined to domestic medication until about 1852 when it entered professional medicine.

Description.—Rhizome horizontal, nearly cylindrical, somewhat branched, 4 to 10 cm. in length, 3 to 13 mm. in diameter; externally weak brown to moderate yellowish brown; upper surface with conical buds, short stem remnants or stem-scars; under and side portions with numerous roots or root-scars; fracture tough; internally, bark pale brown to dark brown, resinous; wood white to light brown, porous; pith large, more or less hollow, light to dark brown.

Roots up to 10 cm. in length and 2 mm. in diameter, externally smooth, or longitudinally wrinkled; fracture short; internally, cortex thick, dark colored; wood cylinder, light colored.

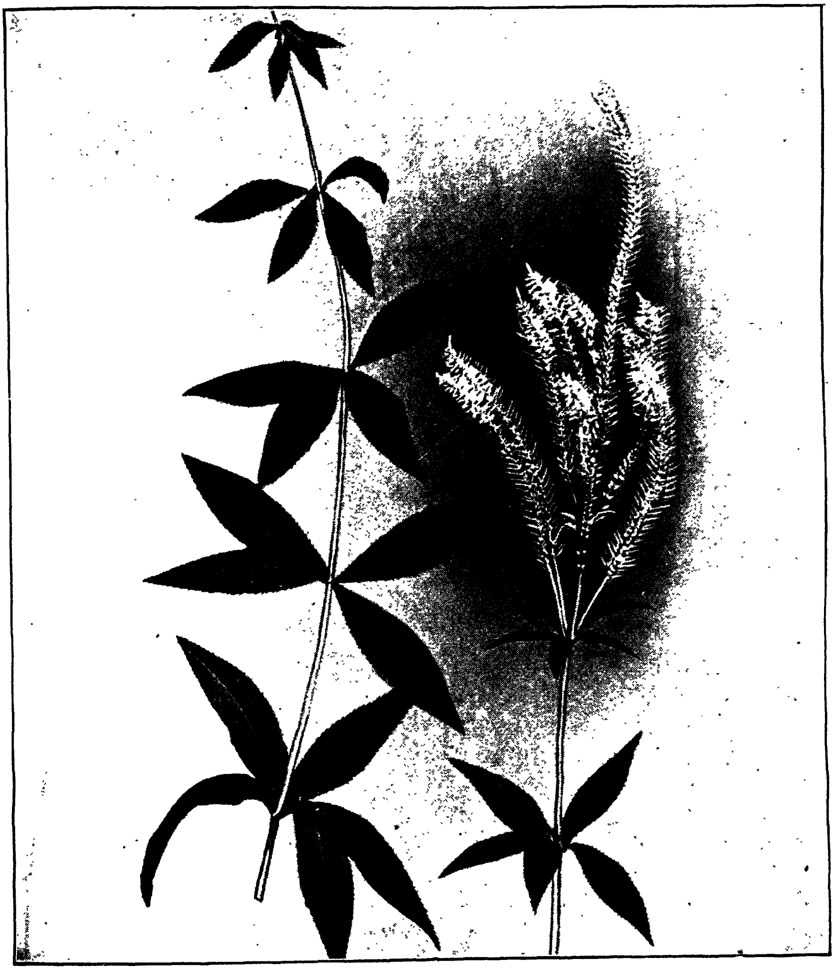


Fig. 328.—Culver's Root (*Leptandra virginica*) showing the verticillate leaves and the long spike-like terminal racemes.

Structure.—See Figure 329 and the National Formulary.

Powder.—Pale brown to light yellowish brown, with a characteristic odor and a very bitter, acrid taste; parenchyma cells containing a light brown or brownish black resin, the latter frequently closely coherent with the starch grains in the cells; starch grains numerous, nearly spheroidal or more or less polygonal, and up to 9 microns in diameter; tracheæ with spiral thickenings or simple or bordered pores; wood fibers with thick lignified porous walls, resembling tracheids; fragments containing a pigment which is colored pink or violet upon the addition of chloral T.S.; epidermal cells of the root having thick lamellated walls.

CONSTITUENTS.—An amorphous substance having an intensely bitter and nauseous taste and yielding on hydrolysis a resinous material and cinnamic

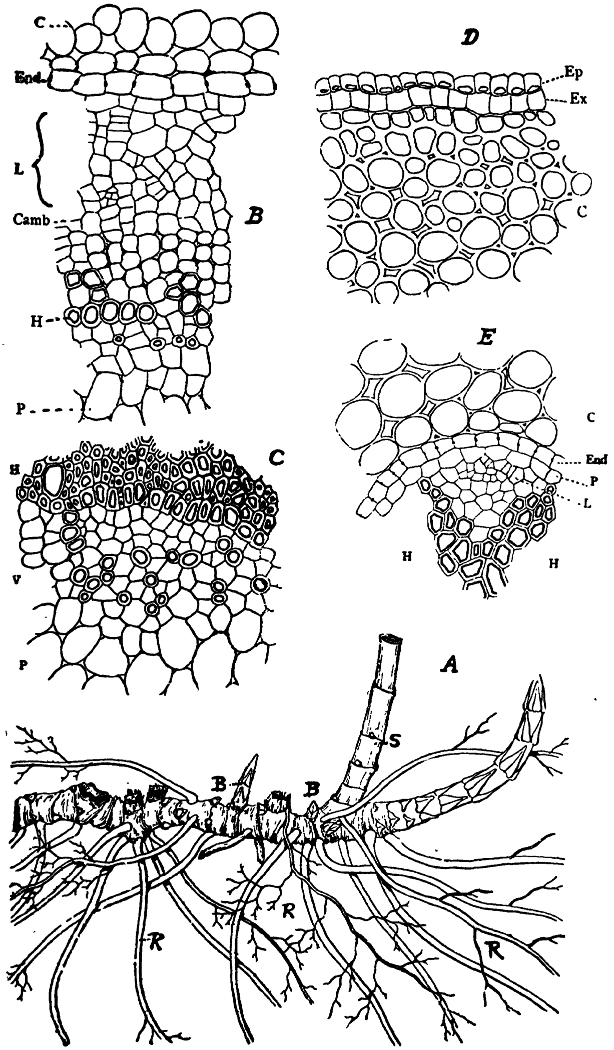


FIG. 329.—Leptandra: *A*, rhizome showing the roots (*R*), buds (*B*), and the base of an aërial stem. *B*, Transverse section of inner portion of a stolon: *C*, Cortex; *End*, endodermis; *L*, a deep strand of phloem having small sieve groups and thin-walled parenchyma; *Camb*, cambium; *H*, primary tracheæ bordering on the pith (*P*). *C*, Transverse section of part of the stele of the main rhizome: *H*, the secondary xylem, showing numerous, thick-walled wood fibers and a single trachea. *D*, Transverse section of outer portion of a root: *Ep*, epidermal cells having thick outer walls; *Ex*, hypodermis; *C*, cortex. *E*, Transverse section of a portion of the root-stele: *C*, cortex; *End*, endodermis; *P*, pericambium; *L*, phloem; *H*, xylem. (After Holm.)

and para-methoxycinnamic acids. Also present are a phytosterol which has been designated verosterol; a volatile oil; tannic acid; a sugar; a resin; *d*-mannitol, and 3:4-dimethoxycinnamic acid. Total ash, 2.59 per cent; acid-insoluble ash, 0.4 per cent.

STANDARDS.—Leptandra contains not more than 5 per cent of attached stem-bases and not more than 2 per cent of other foreign organic matter and yields not more than 6 per cent of acid-insoluble ash.

USES AND DOSE.—Leptandra is a cathartic and an emetic. Average dose, gm.

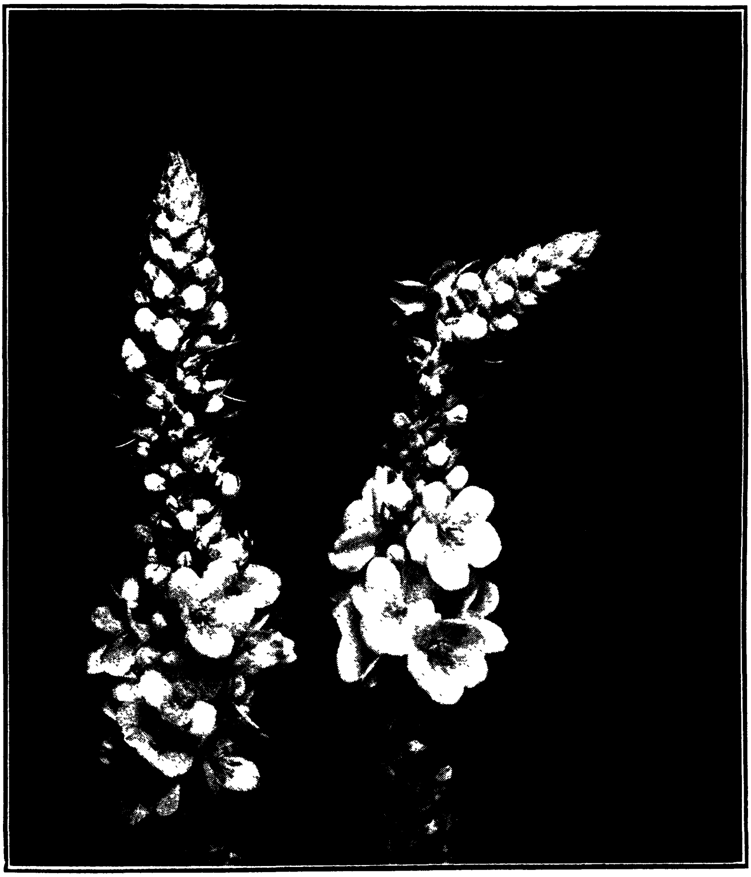


FIG. 330.—*Verbascum phlomoides.* Flowering tops of plants grown in Medicinal Plant Garden, University of Minnesota.

Verbasci Folia or Mullein Leaves (N. F. 1916 to 1936) is the dried leaf of *Verbascum thapsus*, a biennial herb naturalized from Europe and growing in fields and waste places in the eastern and central United States, often becoming a common weed. The leaves are gathered during summer, at the time of flowering of the plant, and carefully dried.

The leaves are elliptical, ovate or obovate, short petiolate, from 6 to 60 cm. in length and 2.5 to 15 cm. in breadth, with an acute or rounded apex, a dentate margin, decurrent base, narrowed into the petiole; pale grayish green and densely woolly-hairy throughout; very thick and rather rough; inodorous; taste mucilaginous and slightly bitter.

Especially characteristic of the powder are the branched multicellular hairs, which consist of an upright, uniseriate main axis of 2 to 8 cells, from which whorls of branch cells arise at the joints, the individual cells being from 150 to 600 microns in length and frequently containing air; glandular hairs 2-celled, consisting of a stalk, from 30 to 65 microns in length and having a nearly spheroidal secreting cell at the summit; epidermal cells strongly undulate, stomata broadly elliptical, about 30 microns in length and having 3 to 5 neighbor cells.

The drug contains an amorphous bitter principle; mucilage; a trace of a volatile oil; and from 1 to 2 per cent of resin, part of which is soluble in ether. Total ash about 10 per cent; acid-insoluble ash 1.8 per cent.

Mullein leaves are demulcent and emollient.

Verbasci Flores or Mullein Flowers (N. F. 1916 to 1936) consists of the dried corolla with adhering stamens, of *Verbascum phlomoides* and *V. thapsiforme*, biennial herbs indigenous to central and southern Europe and western Asia. The former is naturalized to some extent from New England to Kentucky and resembles *V. thapsus* but the leaves are nearly sessile and only slightly decurrent. The corollas, with the adhering stamens, are gathered during dry weather in July or August and carefully dried.

The corollas are zygomorphic, either rotate and about 2 cm. in breadth (*V. thapsiforme*), or somewhat funnel-shaped and about 1.5 cm. in breadth (*V. phlomoides*); golden-yellow when fresh, becoming yellowish brown on drying; dorsal surface pubescent, the lobes being ovate, the 2 upper being smaller than the 3 lower lobes; stamens inserted on the corolla, unequal, the 2 upper being longer and glabrous, while the 3 lower are smaller, the filaments being very pubescent; odor distinct, sweet; taste mucilaginous and sweet.

Mullein flowers contain invert sugar, 10.4 per cent; mucilage; volatile oil; a glucosidal coloring principle; cane sugar, and total ash about 6.5 per cent, with about 1 per cent of acid-soluble ash.

The drug is a demulcent and pectoral.

PEDALIACEÆ, OR SESAME FAMILY

This is a family comprising 16 genera and about 60 species of annual or perennial hairy herbs having simple leaves, usually opposite except that the apical ones are occasionally alternate. The flowers are irregular, pentamerous. The fruit is a capsule, a drupe or rarely a one-seeded nut and the seeds are usually exalbuminous.

The plants are mostly tropical. Histologically they exhibit glandular hairs with heads which are invariably divided by vertical walls only; calcium oxalate, when present, is usually in the form of small solitary crystals.

SESAMUM

Sesamum Seed or Sesame Seed is the seed of one or more cultivated varieties of *Sesamum indicum* Linné.

Sesamum is from the Greek *sesamon*, the original name of the plant; *indicum* pertains to its habitat, India. The plant is an annual herb attaining the height of about one meter, native to southern Asia, but cultivated from Africa to the East Indies and in the West Indies and the southern United States.

The seeds are small, flattened, oval or ovate, smooth and shiny, whitish, yellow or reddish brown; taste sweet and oily. They contain 45 to 55 per cent of fixed oil, 22 per cent of proteins (aleurone) and 4 per cent of mucilage. They are nutritious and form an important food in India. In Europe and America they are used like poppy seed on bread and rolls. The fixed oil is obtained by expression.

Sesame Oil, Teel Oil or Benne Oil (U. S. P. 1820 to 1905; N. F. 1926 to 1947; U. S. P. 1947 to date) is a fixed oil obtained from the seed of one or more cultivated varieties of *Sesamum indicum* Linné.

DESCRIPTION.—Sesame oil is a pale yellow liquid, almost odorless, and with a bland taste. Consult the U. S. Pharmacopœia for constants and tests.

CONSTITUENTS.—Sesame oil contains about 75 per cent of olein. Other constituents are the glycerides of linolic, palmitic, stearic, and myristic acids. It also contains a phenolic substance called sesamol.

STANDARDS.—Sesame oil should be free from cottonseed oil.

USES.—Sesame oil is a nutritive, laxative, demulcent and emollient.

Sesamum, Benne or Sesame Leaves (U. S. P. 1831 to 1882) are the fresh (rarely dried) leaves of *Sesamum indicum* Linné. The leaves are long-petioled, the leaf lamina up to 12 cm. long, ovate or lance-oblong, rather acute apex, entire or toothed or lobed or even with distinct leaflets. The taste is very mucilaginous. Mucilage is the important constituent, for the drug is used principally as a demulcent and to prepare a demulcent drink.

PLANTAGINACEÆ, OR PLANTAIN FAMILY

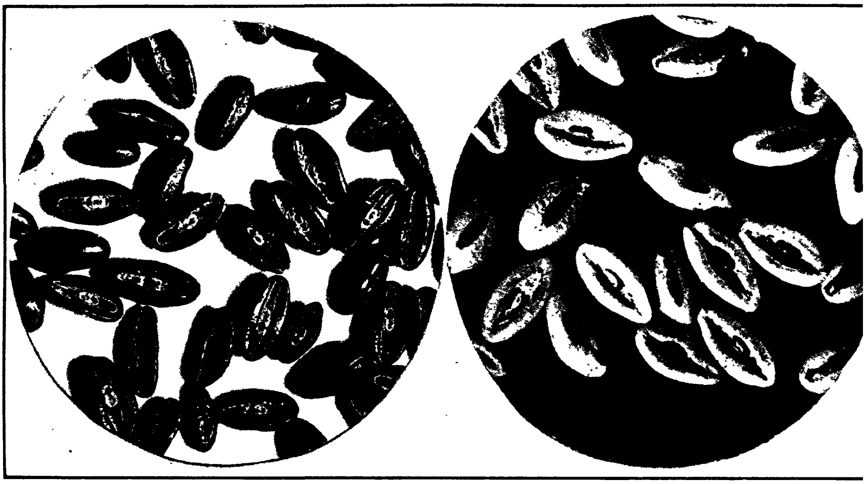
This family includes 203 species of which 200 belong to the genus *Plantago*. The plants are annual or perennial herbs widely distributed throughout the temperate zone. The flowers have 4 sepals and 4 stamens, the corolla also showing 4 divisions. The fruit is a 2-celled pyxis. The family is characterized by glandular hairs, the heads of which, as in the *Labiatæ* and *Verbenaceæ*, are mostly divided by vertical walls only; the stomata resemble those of the caryophylleous type; calcium oxalate is absent and medullary rays are not present in the wood, even in shrubby species. The formation of cork is superficial.

PLANTAGO

Plantago Seed, Psyllium Seed or Plantain Seed (N. F. 1936 to date) is the cleaned, dried, ripe seed of *Plantago Psyllium* Linné, or of *Plantago indica* Linné (*Plantago arenaria* Waldstein et Kitaibel), known in commerce as Spanish or French Psyllium Seed; or of *Plantago ovata* Forskal, known in commerce as Blond Psyllium or Indian Plantago Seed. *Plantago* is from the Latin, meaning sole of the foot and refers to the shape of the leaf; *psyllium* is from the Greek, meaning flea in reference to the color, size and shape of the seed (Fleaseed); *arenaria* is from the Latin *arena*, meaning sand, and refers to the sandy habitat of the plant; *ovata* refers to the ovate shape of the leaf.

Plantago psyllium is an annual, caulescent, glandular, pubescent herb native to the Mediterranean countries and extensively cultivated in France, which country today yields the bulk of our imports of Psyllium seed. *Plantago ovata* is an annual acaulescent herb native to Asia and the Mediterranean countries. The plant is extensively cultivated in India.

In France, planting is done in March, and when the seeds are about three-quarters mature, in August, the field is mowed about dawn, when the dew is heaviest, to prevent scattering of the seed. The plants, partially dried in the sun, are threshed, the seed cleaned and bagged and allowed to fully dry. In Europe the seed have been a domestic remedy since the sixteenth century, but only since 1930 has it been extensively used in America as a popular remedy for constipation.



A *B*

FIG. 331.—Psyllium Seed: *A*, French Psyllium Seed (*Plantago psyllium*); *B*, Indian Plantago Seed (*Plantago ovata*). (Photo by R. S. A.)

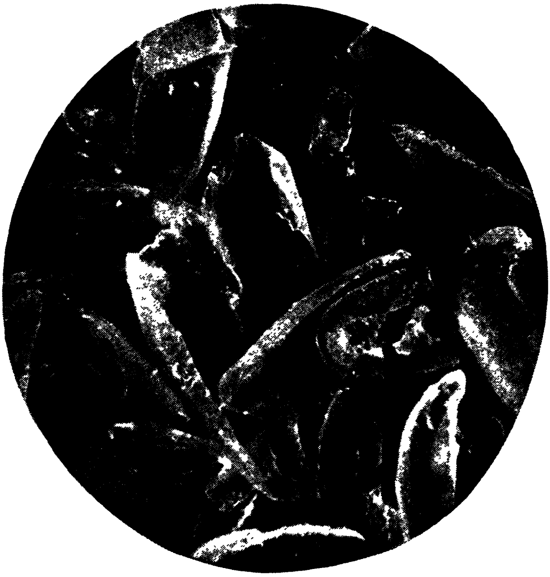


FIG. 332.—Psyllium Seed Husks. The mucilaginous layer of the seed coat separated from blond psyllium seed. (Photograph by P. D. Carpenter.)

DESCRIPTION.—The seed of *P. psyllium* is ovate to ovate-elongate, concavo-convex; mostly from 1.3 to 2.7 mm. in length, rarely up to 3 mm., and from

0.6 to 1.1 mm. in width; light brown to moderate brown, dark brown along the margin, very glossy; the convex dorsal surface exhibiting a transverse groove nearer the broader end, and a longitudinal brown area extending nearly the length of the seed and representing the embryo lying beneath the seed coat; the concave ventral surface with a deep cavity, in the center of the base of which is an oval white hilum.

Seed of *P. indica*, ovate-oblong to elliptical, concavo-convex; from 1.6 to 3 mm. in length, and from 1 to 1.5 mm. in width; externally moderate yellowish brown to dark brown, occasionally somewhat glossy, often dull, rough, and reticulate; the convex dorsal surface with a longitudinal light brown area extending lengthwise along the center and beneath the seed coat, and a median transverse groove, dent, or fissure; the ventral surface with a deep concavity; the edges somewhat flattened and frequently forming a sharp indented angle with the base of the cavity, the latter showing a pale brown to whitish oval hilum.

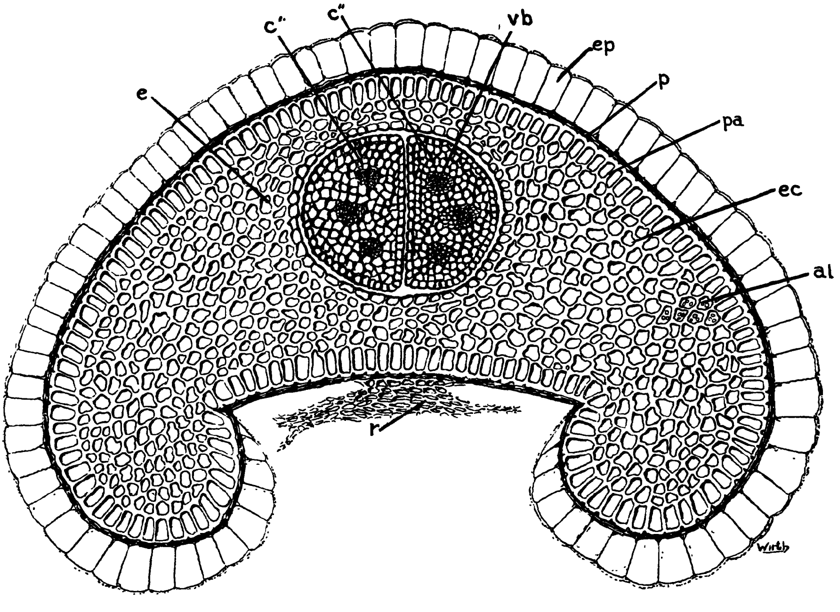


FIG. 333.—*Plantago psyllium.* Median transverse section of the seed showing a seed coat with large epidermal cells (*ep*) whose radial and outer walls break down to form mucilage when brought into contact with water, and a brown pigment layer (*p*) of more or less collapsed cells; a broad endosperm (*e*) having a single outer row of thick-walled palisade cells (*pa*) and irregular inner endosperm cells (*ec*) with thick reserve cellulose walls. The straight embryo lies in the center of the endosperm, the two cotyledons (*c'*, *c''*) being seen in the median transverse section. Three vascular bundles (*vb*) (plerome bundles) extend longitudinally through each cotyledon. The cells of both embryo and endosperm contain fixed oil and aleurone grains (*al*), the latter being rounded, oval or irregular in shape and about 4 microns in diameter. A portion of the raphé (*r*) often remains attached to the seed. Sections of the seeds of *Plantago indica* and of *Plantago ovata* exhibit a similar structure except that in the latter there is no pigment in the seed coat. (Drawing by E. H. Wirth.)

Seed of *P. ovata* broadly elliptical to ovate, boat-shaped; from 2 to 3.5 mm. in length and from 1 to 1.5 mm. in width; pale grayish brown with a pinkish tinge and with a dull surface; the convex surface with a small, elongated, glossy brown spot; the concave surface with a deep cavity in the center of the base of which occurs a hilum covered with a thin, whitish membrane.

Structure.—See Figure 333 and the National Formulary.

Constituents.—Mucilage, about 10 per cent when calculated as pentosans and galactans; fixed oil and protein (aleurone). Total ash about 3 per cent.

Standards and Tests.—Plantago seed contains all of its natural mucilage and not more than 0.5 per cent of foreign organic matter. It yields not more than 4 per cent of total ash and not more than 1 per cent of acid-insoluble ash. When the seed is placed in water the radial and outer walls of the epidermal cells swell to form layers of mucilage about the seed (see Fig. 334). The following test for quality has been devised:

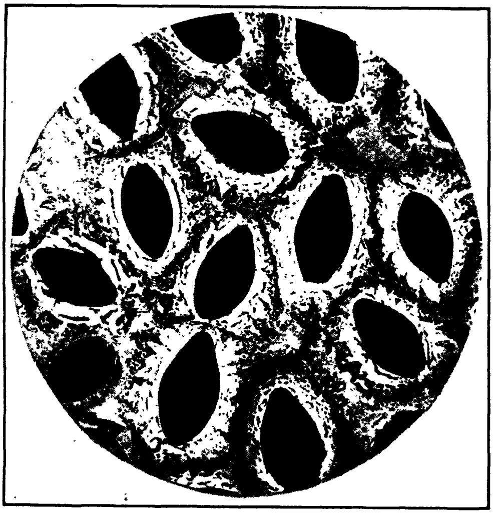


Fig. 334.—Seeds of *Plantago psyllium* placed in water showing the swelling of the mucilage. (Photo by R. S. A.)

Place 1 gm. of plantago seed in a 25 cc. graduated cylinder, add water to the 20 cc. mark and shake the cylinder at intervals during twenty-four hours; allow the seeds to settle for twelve hours and note the total volume occupied by the swollen seeds: the seeds of *Plantago psyllium* occupy a volume of not less than 14 cc., those of *Plantago ovata* not less than 10 cc. and those of *Plantago indica* not less than 8 cc.

Uses and Dose.—Plantago seed is a laxative due to the swelling of the mucilaginous seed coat, thus giving bulk and lubrication. The seeds should be taken with considerable water. Average dose, 8 gm.

Metamucil (NNR) is a mixture containing about 50 per cent of powdered mucilaginous portion (outer epidermis) of blond psyllium seeds (*Plantago ovata*) and powdered anhydrous dextrose, with sodium bicarbonate 0.2 per cent, monobasic potassium phosphate 0.25 per cent, citric acid 0.33 per cent and benzyl benzoate 0.04 per cent. The mucilaginous layer of the seed coat is separated by a physical-chemical process, and is known in commerce as "psyllium seed husks." Combined with the chemicals as indicated above, it is used as an adjunct in the treatment of constipation. It is given in doses of 4 to 7 gm., one to three times a day.

RUBIACEÆ, OR MADDER FAMILY

This is a large family of about 380 genera and 4600 species, most abundant in tropical regions but having representatives in nearly all parts of the world. They vary from herbs to trees; the leaves are usually opposite, stipulate and possess entire margins; the flowers are perfect, the corollas being gamopetalous and of a variety of forms; and the fruit is a capsule, berry or drupe. Among the anatomical features the following are the more prominent. The secretory elements are of a number of forms: (*a*) glandular hairs, consisting of several rows of cells, may occur on the stipules; (*b*) the epidermal cells occasionally contain a resinous secretion; (*c*) cells containing resin are sometimes present in the mesophyll; (*d*) secretory cells having a brownish content are found in the leaves of a number of genera and are probably widely distributed; (*e*) elongated secretory sacs have been observed in *Cinchona, Cascarilla* and other genera; and finally (*f*) a group of secretory cells tending to form internal glands. The fibrovascular bundles are collateral; the walls of the tracheæ have either simple pores or scalariform perforations; and the wood fibers usually possess bordered pores or occasionally simple pores. Calcium oxalate is secreted in a great many different forms. The neighbor cells of the stomata are arranged parallel to the pores. Non-glandular hairs are either unicellular or uniseriate.

ALKALOIDS

At various places throughout the text it has been thought profitable to introduce brief discussions relative to groups of drugs based upon their active constituents. Since the Family *Rubiaceæ* is rich in alkaloids, a discussion of that group is introduced at this point. It is quite impossible to formulate a definition for an alkaloid that would on the one hand limit the substances usually included in this category and on the other hand exclude those substances not usually considered as alkaloids. One of the most common definitions states that an alkaloid is "a nitrogenous base of plant origin having marked physiological action." This is quite in error since some of the alkaloids are not necessarily basic in reaction and many of them possess little or no physiological action. All alkaloids contain one or more nitrogen atoms, which is also true of the proteins. While it is true that most alkaloids are derived from plants, there are substances of animal origin that from any chemical reasoning certainly ought to be included with the alkaloids. A case in point includes ephedrine (of plant origin) and epinephrine (of animal origin) both of which are quite similar in chemical constitution. The best that can be said is that alkaloids are nitrogenous: they are usually of plant origin, frequently basic in character and often have a definite physiological action.

Alkaloids usually contain one nitrogen atom although some like ergotoxine may contain up to five. The nitrogen may exist as a primary amine ($R-NH_2$), a secondary amine as such (R_2NH) or cyclic, a tertiary amine as such (R_3N) or cyclic or a quaternary ammonium hydroxide as such (R_4N-OH) or cyclic. These forms of nitrogen linkage are basic and account for the common basic nature of the alkaloids. Acid amides (neutral) and acid imides (acid) may also be found in the alkaloids.

In spite of the difficulty in definitely characterizing alkaloids by definition they do show a surprizing number of physical and chemical properties in common. For the most part the alkaloids are insoluble or sparingly so in water but form salts (by metathesis or addition) which are usually freely soluble. The free alkaloids are usually soluble in ether or chloroform or other immiscible solvents, in which however, the alkaloidal salts are insoluble. This permits a ready means for the isolation and purification of the alkaloids as well as for their quantitative estimation. Most of the alkaloids are crystalline solids although a few are amorphous and an additional few (coniine, nicotine, sparteine) are liquids. It is interesting to note that the liquid alkaloids have no oxygen in their molecules. Alkaloidal salts are invariably crystalline and their crystal form and habit is often a useful means of their rapid microscopical identification.

The alkaloids, like other amines form double salts with compounds of mercury, gold, platinum and other heavy metals. These double salts are usually obtained as precipitates and many of them are microcrystallographically characteristic. Among the common alkaloidal reagents are Wagner's (iodine in potassium iodide), Mayer's (potassium mercuric iodide), Dragendorff's (potassium bismuth iodide), Hager's (picric acid), Marme's (potassium cadmium iodide), Sonnenschein's (phosphomolybdic acid), gold chloride, mercuric chloride, tannic acid, and many others. The alkaloids usually possess a bitter taste.

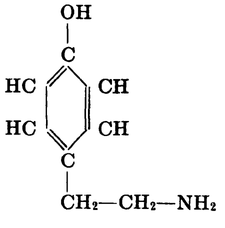
The alkaloids appear to have a restricted distribution in the vegetable kingdom. Among the angiosperms the *Apocynaceæ, Leguminosæ, Papaveraceæ, Ranunculaceæ, Rubiaceæ, Solanaceæ* and *Fumariaceæ* are outstanding for plants yielding alkaloids. The *Labiatæ* and *Rosaceæ* are quite free and the monocotyledons and gymnosperms only rarely contain them. A specific alkaloid is usually confined to a specific plant family, although caffeine and berberine are exceptions to this rule. Alkaloids may occur in various plant parts; in seeds and fruits (nux vomica and black pepper); in leaves (the solanaceous leaves); in rhizomes and roots (aconite, corydalis, hydrastis) and in barks (cinchona, pomegranate).

The names of the alkaloids are obtained in various ways: (1) from the generic and specific names of the plants yielding them (colchicine, belladonnine); (2) from the name of the drug yielding them (ergotoxine); (3) from their physiological activity (emetine, morphine) and occasionally from the discoverer (pelletierine). Sometimes a prefix or suffix is added to the name of a principal alkaloid to designate another alkaloid from the same source (quinine, quinidine, hydroquinine). By agreement, chemical rules designate that the names of all alkaloids should end in "ine".

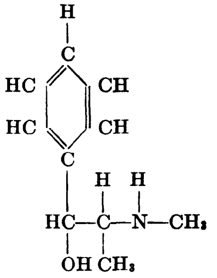
Various schemes for the classification of alkaloids based upon their constitution have been suggested. Because of the wide variation in the constitution of alkaloids, however, none of these are quite satisfactory. A typical and fairly convenient arrangement is as follows:

A. The Group Containing Aliphatic Bases With an Aromatic Nucleus:

Including such compounds as tyramine (p-hydroxyphenylethylamine) from ergot, ephedrine from ephedra and colchicine from colchicum.



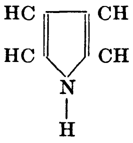
Tyramine



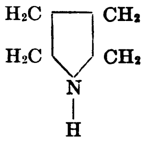
Ephedrine

B. The Pyrrolidine Group:

Pyrrolidine occurs free in small quantities in tobacco and opium and is related to its mother substance pyrrole as follows:

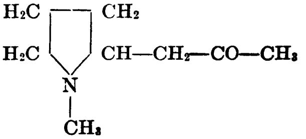


Pyrrole



Pyrrolidine

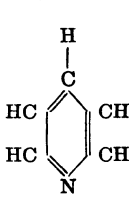
To this group belong such alkaloids as hygrine from *Erythroxylon coca* and stachydrine from *Stachys tuberifera.*



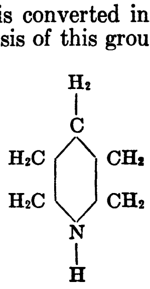
Hygrine

C. The Pyridine Group:

Upon reduction the tertiary base pyridine is converted into the secondary base piperidine. These two nuclei form the basis of this group.

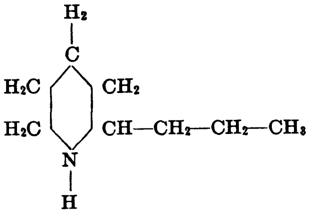


Pyridine

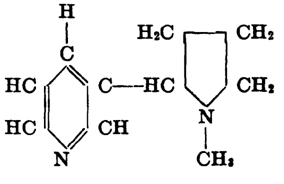


Piperidine

The group is sometimes divided into four sub-groups: (1) derivatives of piperidine including piperine from black pepper (see page 196) and methysticin from kava, (2) derivatives of α-propylpiperidine including coniine from conium; (3) derivatives of nicotinic acid including arecoline from areca (see page 145), and (4) derivatives of both pyridine and pyrrolidine including nicotine from tobacco.



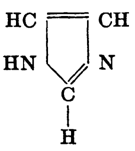
Coniine



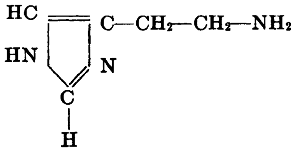
Nicotine

D. The Glyoxaline Group:

Imidazole (glyoxaline) is the principal nucleus in histamine from ergot and pilocarpine from pilocarpus (see formula in the U. S. Pharmacopœia).



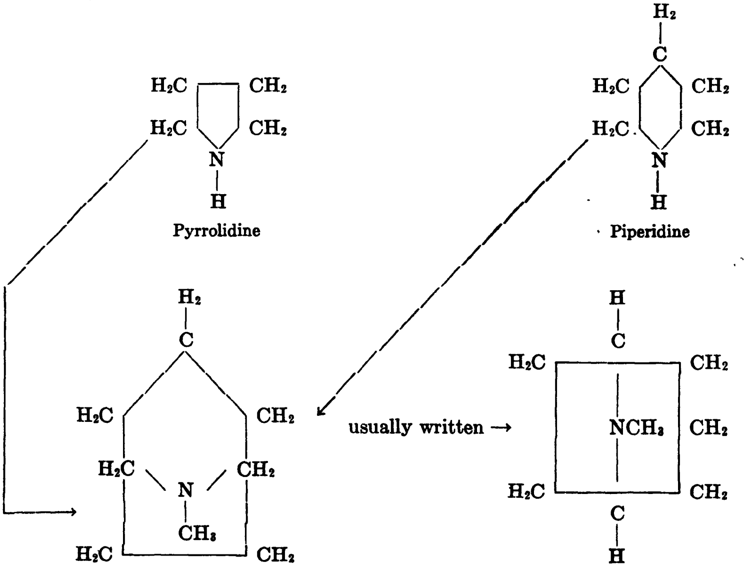
Imidazole



Histamine

E. Alkaloids With Condensed Pyrrolidine and Piperidine Rings:

Tropane is formed when pyrrolidine and piperidine are condensed. Closely related to tropane are tropine (page 554), the principal nucleus of the solanaceous alkaloids, atropine, hyoscyamine, hyoscine and belladonnine, and ecgonine (page 366), the nucleus of cocaine.



Pyrrolidine

Piperidine

Tropane

usually written →

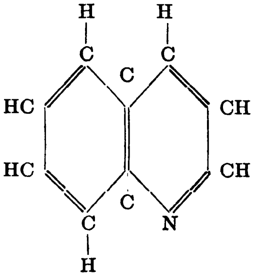
Tropane

F. Derivatives of Quinoline:

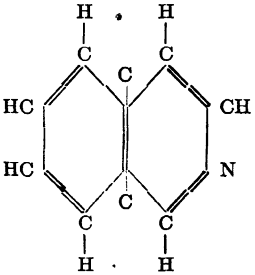
Alkaloids containing quinoline as the principal nucleus include anemonine from *Anemone thalictroides*, galipine from Angostura bark (*Galipea officinalis*) and the cinchona alkaloids, quinine, quinidine, cinchonine and cinchonidine. (See the U. S. P. and N. F. for structural formulæ.)

G. **Derivatives of Isoquinoline:**

Alkaloids containing the isoquinoline nucleus may be divided into two groups: (1) papaverine, narcotine, cotarnine, narcine and certain others of the opium group, and (2) the hydrastis group including hydrastine, berberine and canadine. (See U. S. P. and N. F. for structural formulæ.)



Quinoline



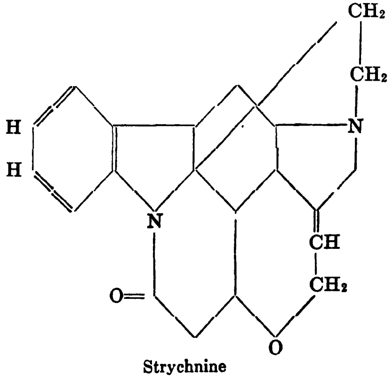
Isoquinoline

H. **Phenanthrene:**

The opium alkaloids, morphine, codeine and thebaine have a phenanthrene nucleus. (See U. S. Pharmacopœia for structural formula.)

I. **Indole Derivatives:**

Certain alkaloids upon distillation with zinc dust yield indole. It is natural therefore to assume that they possess an indole ring as part of their structure. Strychnine and brucine from nux vomica and physostigmine from physostigma belong to this group. Strychnine and brucine contain in addition a quinoline nucleus and many authors classify them in the quinoline group. The following formula for strychnine is now generally accepted:

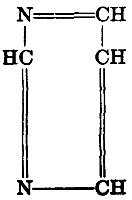


Strychnine

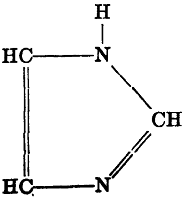
Brucine is dimethyoxystrychnine, in which the methoxy groups replace the two hydrogen atoms indicated in the above formula. For the formula of physostigmine see the U. S. Pharmacopœia.

J. **The Purine Bases:**

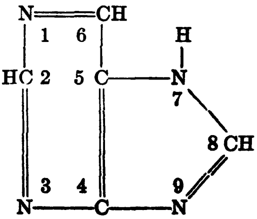
The purine nucleus is constructed by a "condensation" of the pyrimidine and imidazole (glyoxaline) nuclei.



Pyrimidine



Imidazole



Purine

Xanthine is 2,6 dioxypurine; caffeine is 1,3,7 trimethylxanthine, theophylline is 1,3, and theobromine 3,7 dimethylxanthine. These alkaloids are found in coffee, tea, cacao, kola, maté and guarana.

K. **Alkaloids of Unknown Constitution:**
The constitution of a number of alkaloids has not as yet been definitely established. Among these are aconitine from aconite, delphinine from larkspur, jervine and protojervine from veratrum viride, cevadine from sabadilla seed, lobeline from lobelia, the curare alkaloids from *Chondrodendron tomentosum*, sanguinarine from sanguinaria and many others.

As with most attempts at chemical classification some alkaloids do not fall satisfactorily into any of the above groups while others can be classified in more than one group.

CINCHONA

Cinchona, Cinchona Bark or Peruvian Bark (U. S. P. 1820 to 1942; N. F. 1942 to date) is the dried bark of the stem or of the root of *Cinchona succirubra* Pavon et Klotzsch or its hybrids, known in commerce as Red Cinchona; or of *Cinchona Ledgeriana* (Howard) Moens et Trimen, *Cinchona Calisaya* Weddell, or hybrids of these with other species of *Cinchona*, known in commerce as Calisaya Bark or Yellow Cinchona.

Cinchona Flava, Yellow Cinchona, Calisaya Bark or Yellow Bark (U. S. P. 1820 to 1894, as Cinchona 1894 to 1942; N.F. 1942 to date) is the dried bark of *Cinchona Calisaya* Weddell.

Cinchona Pallida, Pale Cinchona, Pale Peruvian Bark, Loxa Bark or Crown Bark (U. S. P. 1820 to 1882, as Cinchona 1882 to 1916) is the dried bark of *Cinchona officinalis* Hooker.

Cinchona Rubra, Red Cinchona, Red Peruvian Bark or Red Bark (U. S. P. 1820 to 1926, as Cinchona 1926 to 1942; N.F. 1942 to date) is the dried bark of *Cinchona succirubra* Pavon.

Cinchona was named in honor of the Countess of Chinchon, wife of the Viceroy of Peru; *succirubra* is Latin meaning "red juice;" *calisaya* is the Spanish and Indian name in Peru for the bark of a tree; *ledgeriana* is named in honor of Charles Ledger who introduced *Cinchona* into the East Indies. The plants are trees indigenous to the Andes of Ecuador and Peru at an elevation of 3000 to 9000 feet, and are cultivated in the East Indies and India. There are 36 known species and hybrids of *Cinchona.*

Just before the Second World War, Java supplied over 90 per cent of the world consumption of this important drug. The Japanese cut off this supply from the world, and several valuable antimalarial agents were developed during the war to take the place of cinchona. Also cultivation of cinchona trees was undertaken in several other countries in Central and South America.

Cultivation gives opportunity to select seed from plants producing high-quality bark; also to hybridize one choice strain with another. Thus, *Cinchona ledgeriana-calisaya* produces a higher yield of alkaloids than either of the parent species. Selected seed planted in seed beds give plants suitable for transplanting when two years old. They are planted in the fields but a few feet apart; the stems tend to grow tall, lower branches tend to die and drop off, the tree crowns are close together, hence shade the trunks, and shade is favorable to the production of quinine. Trees six to nine years old possess the maximum amount of alkaloids in the bark; such trees have produced but a thin cork (the cork is inert); they can be easily pulled from the soil with tractors; the fresh bark of trunk and roots is easily removed by hand; and when well dried it may have an alkaloidal content three times as great as the bark from an old tree will yield.

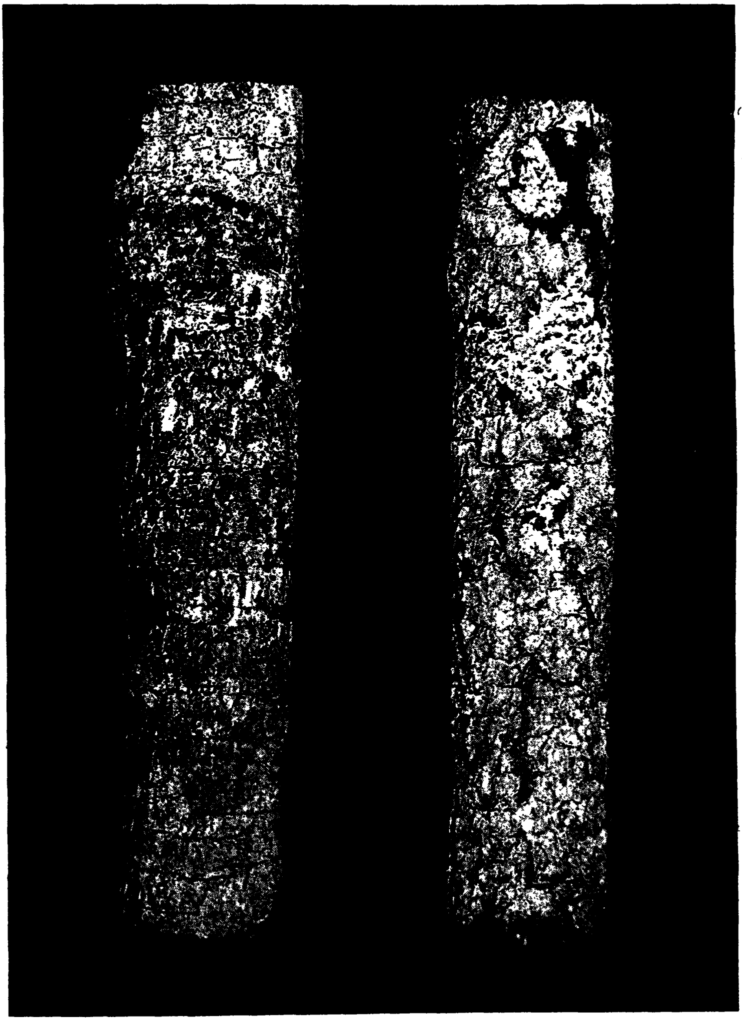


FIG. 335.—Typical specimens of *Cinchona succirubra* bark from Java. (From a photograph by Powers-Weightman-Rosengarten Co., Philadelphia.)

The bark of the stem is usually used in the manufacture of galenicals, while the root bark is used for the extraction of the alkaloids, especially quinine.

For the history of Cinchona, which is lengthy and filled with romance, the student should read Lloyd's History of Pharmacopœial Drugs. The natives of Peru seem to have been unacquainted with the properties of the drug, its bitter taste rather inspiring them with fear. Although Peru was discovered in 1513 it is not until 1638 that the story begins. Tradition has it that an Indian, overcome with fever was forced to

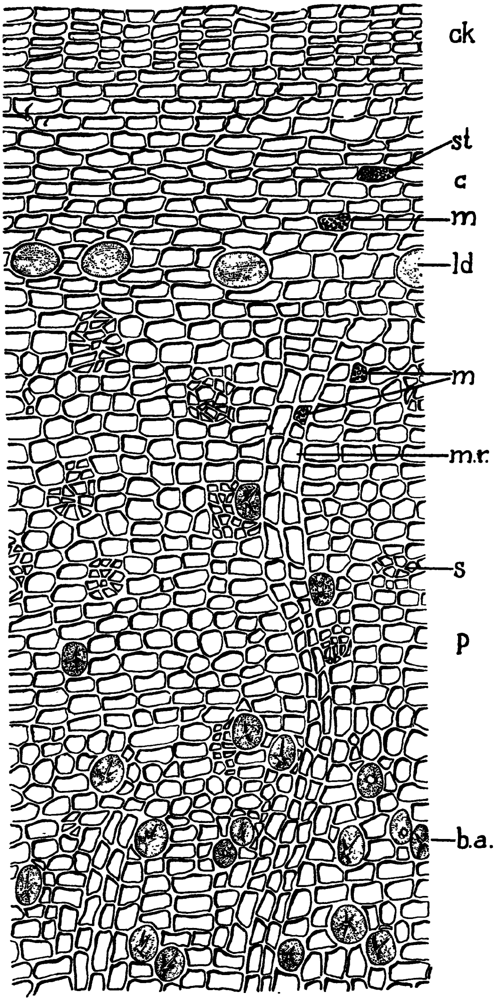


FIG. 336.—*Cinchona calisaya:* transverse section of the bark showing a cork (*ck*) of numerous layers of rectangular cells; a cortex (*c*) consisting of brown-walled parenchyma containing starch (*st*) and occasional microcrystals (*m*) and circular or oval laticiferous ducts (*ld*) up to 120 microns in diameter; a broad phloem (*p*) interspersed by medullary rays (*m.r.*) from 1 to 3 cells in width; phloem patches containing numerous bast fibers (*b.a.*) isolated or in small groups, and occasional patches of sieve tissue (*s*). (Drawing by Edward Fried.)

drink stagnant water in which fallen cinchona trees had macerated for some time. An Indian medicine man near Loxa taught a Jesuit missionary the use of the drug, who in turn taught others, among them Canizares the corregidor of Loxa. Canizares sent the bark to Juan de Vega, who at that time was treating the Countess Ana de Osorio, wife of the Count of Chinchon, and Viceroy of Peru, for tertian fever. The Countess recovered and shortly thereafter introduced the bark into Europe. The use of cinchona was further spread through the efforts of the Jesuit Order. For the next half century or more Europe seethed with a controversy over cinchona, the drug being widely condemned on one hand and praised on the other. Early names for the drug were Countess Bark, Jesuit's Bark and Peruvian Bark. It is interesting to note that Linnaeus, in naming the genus, desired to honor the Countess but omitted the second letter in the name, which error has continued to the present day. The tree yielding cinchona bark was unknown until 1737. In 1854 the Dutch began its introduction into Java and in 1860 the English introduced it into India.

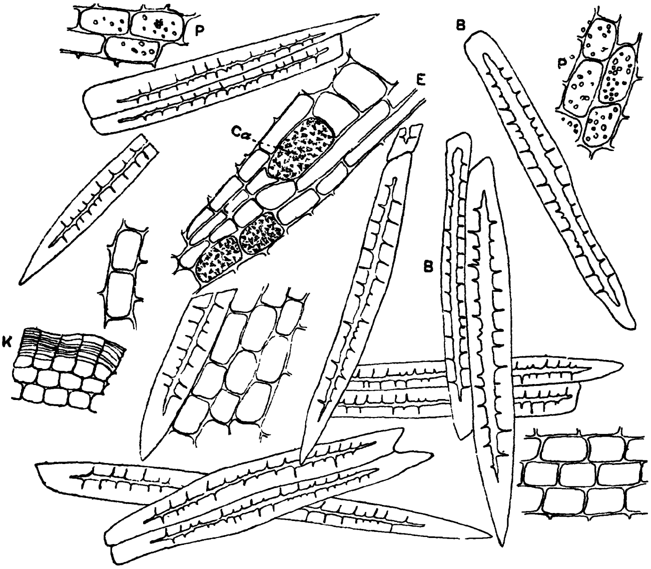


FIG. 337.—Powdered Cinchona: brown; bast fibers (*B*) spindle-shaped, yellowish, 0.300 to 1.350 mm. in length and 50 to 150 microns in width, with thick, strongly lignified, lamellated walls having slit-like, oblique pores; sphenoidal microcrystals (*Ca*) numerous but very minute; parenchymatous cells, (*P*) with reddish brown tannin masses; starch grains relatively few, either single or 2- to 5-compound, the individual grains from 3 to 20 microns in diameter; sieve tissue (*E*); and cork (*K*) of small rectangular, thin-walled cells with brown contents.

DESCRIPTION.—In fragments, coarse powder or in double quills from 15 to 20 mm. in diameter, bark 2 to 8 mm. in thickness; outer surface weak reddish brown to moderate yellowish brown, with grayish patches of foliaceous lichens on the stem bark; more or less roughened with corky ridges or protuberances and with transverse fissures, in red cinchona the fissures have sloping sides, are seldom numerous and rarely intersect; in yellow cinchona they are numerous, have nearly vertical sides and frequently intersect longitudinal fissures; inner surface reddish brown, distinctly striate; fracture short and granular in the periderm, but in the inner bark with projecting bast fibers; odor distinct; taste astringent and very bitter.

STRUCTURE AND POWDER.—See Figures 336, 337 and the National Formulary.

CONSTITUENTS.—The alkaloids are chiefly formed in the parenchyma cells of the middle layers of the bark. Cinchona contains some 25 closely related alkaloids, of which the most important are quinine, quinidine, cinchonine and cinchonidine, the average yield being 6 to 7 per cent, of which from one-half to two-thirds is quinine in the yellow barks, whereas in the red barks, cinchonidine exists in greater proportion; specimen pieces have yielded as high as 18 per cent of total alkaloids. Other constituents of cinchona are: quinic acid, from 5 to 9 per cent, which forms colorless rhombic prisms and yields a sublimate consisting of golden crystals of quinone on treatment with manganese peroxide and sulfuric acid; quinovin, an amorphous, bitter glucoside, to the amount of 0.11 to 1.74 per cent; cinchotannic acid, from 2 to 4 per cent, which decomposes into the nearly insoluble cinchona red, occurring in red barks to the extent of 10 per cent; considerable starch. Total ash, about 2.55 per cent, with 0.15 per cent of acid-insoluble ash. The red color in cinchona bark is due to an oxydase similar to that which causes the darkening of fruits when cut. If the fresh bark is heated in boiling water for thirty minutes and then dried it does not become red.

STANDARDS AND TESTS.—See the National Formulary.

In commerce, cinchona bark is priced very largely on the basis of its total alkaloid content and frequently on its quinine content.

USES AND DOSE.—Cinchona is a tonic, an antiperiodic and a febrifuge. It frequently produces derangement of the sense of hearing, sometimes, too, that of sight. Average dose, 1 gm.

Cinchona officinalis yielding **Cinchona Pallida Bark** is a shrub indigenous to Ecuador, and is the species first discovered. It is cultivated in nearly all the large cinchona plantations. The bark is usually in small, dark-colored quills. It contains up to 4 per cent of total alkaloids, one-half to one-third of which is quinine.

Cuprea Bark is obtained from *Remijia purdieana* and *R. pedunculata*, of central and southern Colombia. It has a copper-red color, is hard, compact and heavy, contains numerous transversely elongated stone cells and 2 to 6 per cent of alkaloids, of which one-third may be quinine. Cinchonidine has never been isolated from this bark. Cuprea bark also contains caffeate of quinine and caffeic acid, of which there is about 0.5 per cent and which closely resembles the same acid obtained from caffeotannic acid in coffee.

THE CINCHONA ALKALOIDS

Cinchonidine, $C_{19}H_{22}ON_2$, stereoisomeric with cinchonine, is an alkaloid from cinchona, about 0.4 per cent from cultivated bark up to 3 per cent from native bark. It occurs in white, very bitter crystals very slightly soluble in water but readily so in alcohol, chloroform and dilute acids. Some 15 commercial salts of cinchonidine are listed.

Cinchonidine Sulfate (U. S. P. 1882 to 1936; N. F. 1936 to date) occurs in white, silky, acicular crystals, efflorescent in dry air and darkening when exposed to light. It is an antiperiodic, a bitter tonic, etc., but weaker than quinine sulfate. It is used as an antirheumatic for neuralgia, sciatica and rheumatism; as an antispasmodic in heroic doses for whooping cough, and as a tonic.

Cinchonine, $C_{19}H_{22}ON_2$ (U. S. P. 1882 to 1905) is an alkaloid stereoisomeric with cinchonidine. It was discovered in 1811 by Gomez in cinchona and is present in from 0.3 to 1 per cent. It occurs as white to yellow, bitter needles or prisms, and should be protected from light. Ten of its salts are listed commercially.

Cinchonine Sulfate (U. S. P. 1863 to 1926; N. F. 1926 to date) occurs as colorless, lustrous, very bitter crystals, permanent in air, but affected by light. It is rather soluble in water, alcohol and chloroform. It is used like quinine sulfate, though somewhat weaker.

Quinidine, $C_{20}H_{24}O_2N_2$ (N. F. 1916 to 1936) is a stereoisomer of quinine, and present in cinchona barks to the extent of 0.25 to 1.25 per cent. It occurs as white crystals or crystalline powder, slowly darkening on exposure to light. It is readily soluble in alcohol, methanol, ether, chloroform and dilute acids. Eight salts of quinidine are listed commercially.

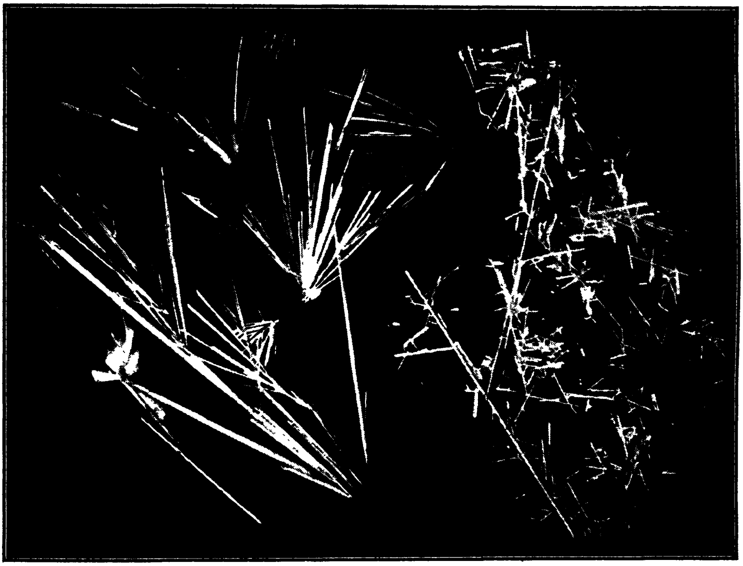


FIG. 338.—Quinine sulfate: long orthorhombic needles from a dilute alcoholic solution.

Quinidine Sulfate (U. S. P. 1882 to 1905, 1936 to date) occurs in white, very bitter, fine crystals, readily soluble in water, alcohol, methanol and chloroform. It is an antiperiodic and protoplasmic poison; it is used particularly to inhibit auricular fibrillation, in an average dose of 0.2 gm.

Quinine, $C_{20}H_{24}O_2N_2$ (U. S. P. 1882 to 1942; N. F. 1942 to date) occurs as white, odorless, bulky, very bitter crystals or crystalline powder; it darkens on exposure to light, and effloresces in dry air. It is freely soluble in alcohol, ether and chloroform, but slightly soluble in water. Fifty-four of its salts are commercially listed.

Quinine Sulfate (U. S. P: Impure quinine sulfate, 1831 to 1842; Pure, 1842 to date) occurs in white, odorless, bitter, fine needle-like crystals;

usually lusterless. It becomes brownish on exposure to light. It readily loses some of its 8 mols of crystallization water when exposed to dry air. It is not readily soluble in water, alcohol, chloroform or ether.

The drug is a protoplasmic poison, especially for protozoa; a specific antimalarial; an antiseptic; an antipyretic and a tonic.

The following quinine salts have been recognized in the U. S. Pharmacopœia or the National Formulary:

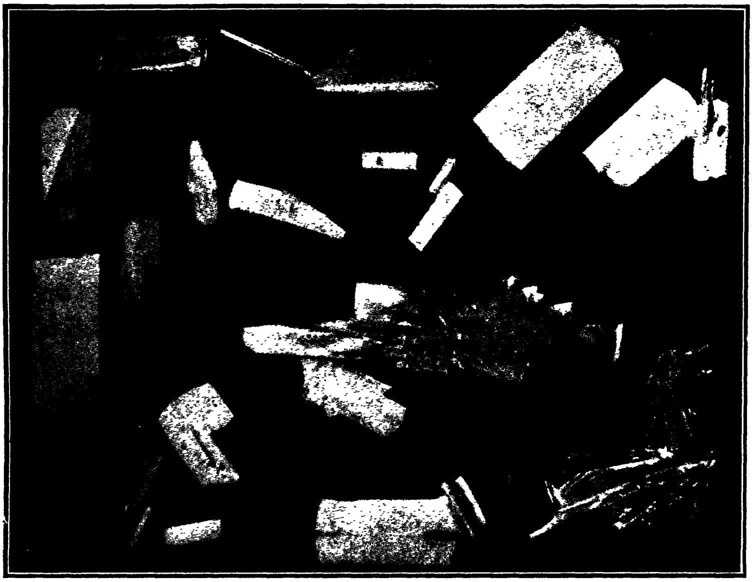


FIG. 339.—Cinchonine sulfate: orthorhombic crystals from a saturated aqueous solution.

Quinine Bisulfate or **Quinine Acid Sulphate** (U. S. P. 1882 to date).

Quinine Dihydrochloride (U. S. P. 1916 to date).

Quinine Ethylcarbonate or **Euquinine** (U. S. P. 1926 to 1947; N. F. 1947 to date).

Quinine and Urea Hydrochloride (U. S. P. 1916 to 1947; N. F. 1947 to date).

Quinine Glycerophosphate (N. F. 1916 to 1926).

Quinine Hydrobromide (U. S. P. 1882 to 1936; N. F. 1936 to date).

Quinine Hydrochloride (U. S. P. 1882 to 1936; N. F. 1936 to 1942; U. S. P. 1942 to date).

Quinine Hypophosphite (N. F. 1916 to 1926).

Quinine Phosphate (N. F. 1936 to date).

Quinine Salicylate (U. S. P. 1905 to 1926; N. F. 1936 to date).

Impure Quinine Sulfate (U. S. P. 1831 to 1842).

Quinine Sulfate (U. S. P. 1842 to date).

Quinine Tannate (U. S. P. 1916 to 1936).
Quinine Valerate (Valerianate) (U. S. P. 1863 to 1905; N. F. 1916 to 1926).

Totaquine (U. S. P. 1942 to date).

The more readily soluble quinine salts are the Bisulfate, Dihydrochloride, Hydrochloride, and Quinine and Urea Hydrochloride, which are used for intravenous injection. Others, such as Quinine Tannate, are so insoluble in the saliva as to greatly reduce the bitter taste. Some have rather specific uses; such as Quinine Oleate as a preventive of sunburn and *x*-ray burn; also, in dilute solution in volatile solvents, for moth-proofing fabrics; Quinine Salicylate is a pronounced antiseptic, especially on the skin; Quinine Valerate is used for nervous headaches and hysteria; Quinine and Urea Hydrochloride is a valuable local anesthetic.

The dosage of quinine salts for the treatment of malaria in adults should never be less than 1 gm. daily, better 1.3 gm. daily; for quartan and malignant malaria, 2 gm. daily should be used. Doses in excess of this are dangerous. A dosage of 0.1 to 0.3 gm. of quinine daily as a preventive of malaria is considered as unsatisfactory; malarial protozoa tolerant to quinine tend to develop. Daily doses of 0.2 to 0.4 gm. as a tonic or as an analgesic in the treatment of colds, are used extensively.

Quinine or Quinidine in solution in dilute sulfuric acid show a characteristic blue fluorescence. When 2 or 3 drops of bromine T.S. are added to 5 cc. of an aqueous solution of a quinine or quinidine salt, and this followed by 1 cc. of ammonia T.S., the liquid acquires an emerald green color, due to the formation of thalleioquin, a very characteristic reaction, capable of detecting quinine or quinidine in a dilution of 1 to 20,000.

IPECAC

Ipecac (U. S. P. 1820 to date) consists of the dried rhizome and roots of *Cephaëlis Ipecacuanha* (Brotero) A. Richard, known in commerce as Rio or Brazilian Ipecac (U. S. P. 1820 to date), or of *Cephaëlis acuminata* Karsten, known in commerce as Cartegena, Nicaragua or Panama Ipecac (U. S. P. 1905 to date). Ipecac yields not less than 2 per cent of the ether-soluble alkaloids of Ipecac.

Cephaëlis is from two Greek words, meaning "head" and "to collect or roll up," referring to the inflorescence; *Ipecacuanha* is Portuguese from the Brazilian Indian *ipe-kaa-guene,* meaning "a creeping plant that causes vomiting;" *acuminata,* refers to the acute apex of the leaf.

The plants are low straggling shrubs with slender rhizomes bearing annulated wiry roots. *C. Ipecacuanha* is indigenous to Brazil and has been cultivated to a limited extent in the Malay States. The commercial supply is from Matto Grosso, Brazil. The drug is gathered during the dry season and dried rapidly in the sun for two or three days. *C. acuminata* is indigenous to the northern portions of Columbia, and up into Panama and Nicaragua. It is exported from Cartegena and Savanilla. Apparently ipecac was used by the South American Indians. The first mention of the drug was by a Jesuit friar in 1601. The drug was introduced into Europe by Le Gras in 1672 and by 1690 was well known in medicine.

DESCRIPTION.—**Rio or Brazilian Ipecac**: roots cylindrical, sharply flexuous or curved, 3 to 15 cm. in length, 1 to 4 mm. in diameter; externally reddish brown to dark brown, smooth or closely annulated, sometimes transversely fissured, the fissures with vertical sides, occasional rootlets or rootlet scars; portions of the annulated roots or even whole roots may be thin and smooth; bark of thin root about one-ninth of whole diameter, of annulated root about two-thirds of whole diameter, and easily separable from the dark yellow, non-porous, fibrous wood.

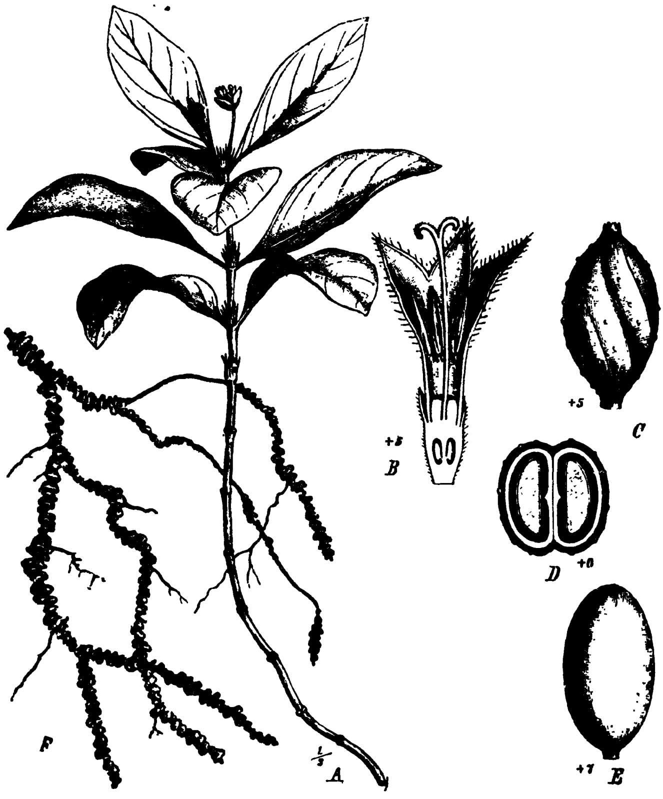


Fig. 340.—Ipecac plant [*Cephaëlis* (*Uragoga*) *Ipecacuanha*]: *A*, flowering shoot; *B*, flower in longitudinal section; *C*, fruit; *D*, fruit in transverse section; *E*, seed; *F*, annulate root. (After Schumann.)

Cartagena Ipecac closely resembles the Rio ipecac, but the roots are uniformly thicker (4 to 7 mm. in diameter), grayish, grayish brown, or reddish brown in color, and the annulations are less pronounced.

Ipecac Stems are usually more slender, 1 to 1.5 mm. in diameter, nearly smooth or longitudinally wrinkled; bark 0.1 mm. in thickness, with bast fibers either single or in groups; pith distinct, 0.5 mm. in diameter.

Structure and Powder.—See Figures 341, 342 and the U. S. Pharmacopœia.

Constituents.—Ipecac contains three alkaloids (2 to 3 per cent)—emetine, cephaëline and psychotrine, contained chiefly in the bark, which makes up about 90 per cent of the drug; ipecacuanhic acid, 2.25 per cent, with which the alkaloids are combined; a glucoside resembling saponin; starch about 40 per cent. Total ash 3.85 per cent; acid-insoluble ash about 1 per cent.

The alkaloids in Rio Ipecac total but little over 2 per cent (about one-third cephaëline and two-thirds emetine); in Cartagena Ipecac alkaloids total 2.5 per cent or more (about four-fifths cephaëline and one-fifth emetine).

Uses and Dose.—Ipecac is an emetic, an expectorant and (often admixed with opium) a diaphoretic. Average dose: emetic, 0.5 gm.; expectorant or diaphoretic, 60 mg.

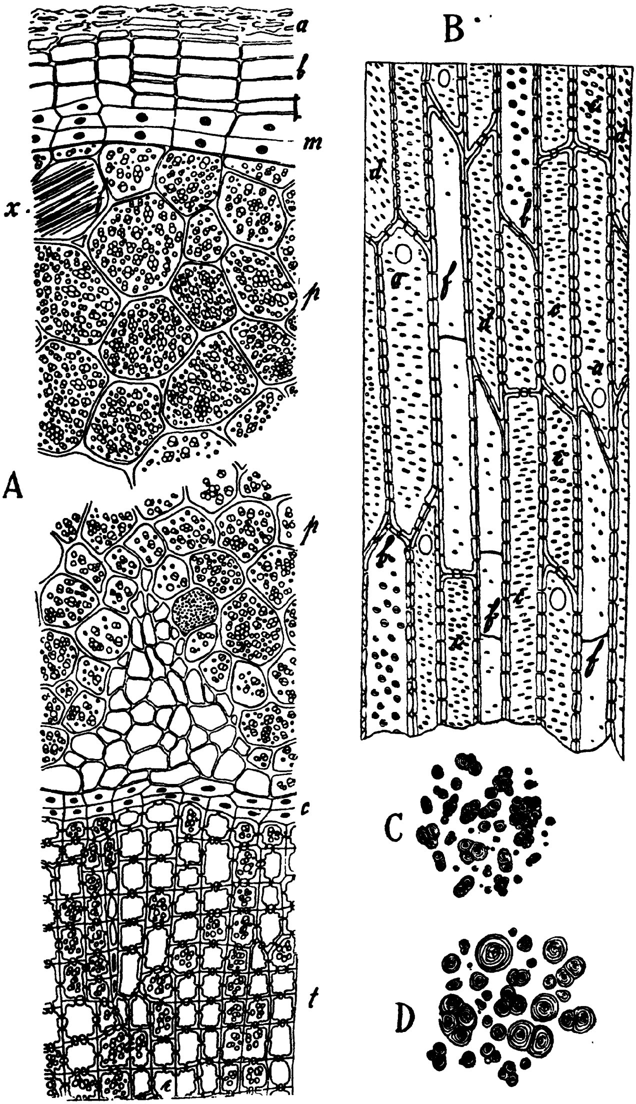


Fig. 341.—Ipecac: *A*, transverse section of Rio Ipecac showing outer layers of cork (*a*); cork cells (*b*); phellogen (*m*); parenchyma containing starch (*p*); raphides (*x*); cambium (*c*); tracheids (*t*). *B*, Longitudinal section of a portion of the wood showing trachea-like tracheids (*a*); tracheids with bordered pores (*b*), linear pores (*c*) and oblique linear pores (*d*); transition tracheids (*e*); tracheids with delicate pores (*f*). *C*. Starch grains of Rio Ipecac. *D*, Slightly larger starch grains of Cartagena Ipecac. (After Schneider.)

Emetine or Methyl Cephaëline, $C_{29}H_{40}O_2N_2$, is an alkaloid obtained from Ipecac or prepared synthetically by methylation of cephaëline. It was discovered by Pelletier in 1817. It occurs as a white, amorphous powder, becoming darker on exposure to light. It forms crystalline salts, of which several are commercially listed.

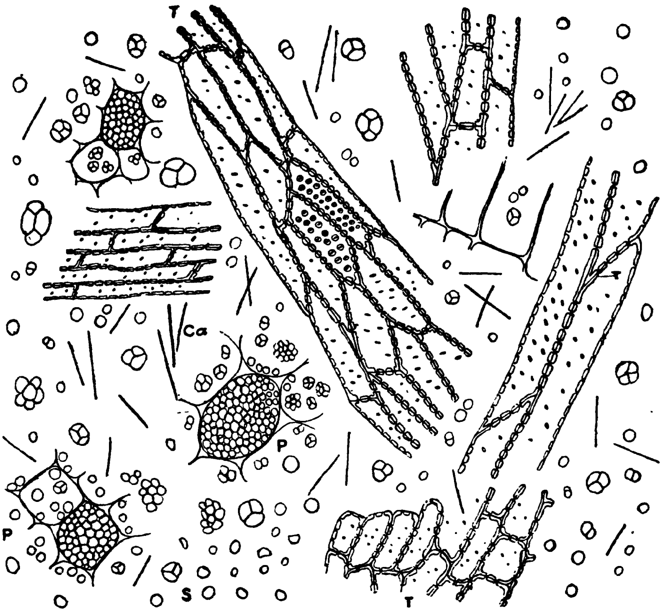


FIG. 342.—Powdered Rio Ipecac: light brown; starch grains, numerous, 2- to 7-compound, the individual grains spheroidal or polyhedral, from 3 to 15 microns in diameter: calcium oxalate (*Ca*) in raphides up to 56 microns in length; tracheids (*T*) having either bordered pores or oblique slit-like pores. The stem bark shows a few, slightly elongated stone cells, from 30 to 45 microns in length, having thick lignified walls and simple branching pores. Starch grains of Cartagena Ipecac, up to 20 microns in diameter.

Emetine Hydrochloride (U. S. P. 1916 to date) is a hydrated hydrochloride of emetine, containing from 4 to 5 mols of water. It occurs as a white, odorless, crystalline powder, becoming yellowish on exposure to light. It is freely soluble in water or in alcohol.

The drug is an expectorant and an emetic, but it is used principally as an amebicide in amebic dysentery and in pyorrhea alveolaris and other amebic diseases. Expectorant dose, about 3 mg.; emetic dose, 10 mg.; amebicide dose, intramuscular, daily, 60 mg., for not to exceed ten days.

Cephaëline, $C_{28}H_{38}O_4N_2$, is an alkaloid obtained from Ipecac, and occurs as white, fine, interlacing needles, darkening on exposure to light. It is insoluble in water, but soluble in dilute acids, alcohol or chloroform.

Cephaëline Hydrochloride is less sensitive to light and readily soluble in water. It is used as an expectorant and an emetic, more active than emetine and possibly more toxic. Dose, as emetic, 5 to 10 mg.

Psychotrine, $(CH_3O)_3C_{25}H_{26}N_2.OH$, an alkaloid obtained from Ipecac, occurs as white to yellow, light-sensitive crystals.

With Frohde's reagent for alkaloids (0.1 gm. sodium molybdate in 100 cc. of sulfuric acid): emetine gives a dirty green color; cephaëline causes a purple color and psychotrine a purplish tinge. Upon the addition of hydrochloric acid, the emetine and psychotrine solutions become bright green, and cephaëline a deep blue.

ALLIED PLANTS.—Several plants of *Rubiaceæ* and of other families produce roots that may resemble Ipecac and that possess emetic properties, but none of them contain emetine.

Undulated Ipecac is the dried root of *Richardia scabra* (Houst.) Linné (*Richardsonia scabra* Linné), a plant growing in tropical and subtropical America, with an undulate, annulate root, the bark of which is nearly as thick as the yellowish, soft wood. It has simple and compound starch grains from 20 to 40 microns in diameter.

Striated Ipecac is the dried root of *Cephaëlis emetica,* a plant growing in South America, with a dark purplish brown root, with a few transverse fissures and a thick bark in which starch is absent.

American Ipecac or Gillenia (U. S. P. 1820 to 1882) and **Indian Physic or Gilleniæ Trifoliatæ Radix** (U. S. P. 1831 to 1842) are the roots of *Gillenia stipulata* and *G. trifoliata* respectively (Fam. *Rosaceæ*). The roots somewhat resemble ipecac root; the American Ipecac root has thinner bark with numerous resin cells, and Indian Physic root is not annulate.

Euphorbia Ipecacuanha or Ipecac Spurge (U. S. P. 1820 to 1882) and **Euphorbia Corollata, Purging Root or Emetic Root** (U. S. P. 1820 to 1882) are the dried roots of *Euphorbia Ipecacuanha* and *E. corollata* respectively (Fam. *Euphorbiaceæ*). These roots (see page 399) are much larger than and do not resemble Ipecac root. They are strongly emetic.

Ionidium, White Ipecac or White Ligneous Ipecac (Fam. *Violaceæ*) is the dried root of *Hybanthus* (*Ionidium*) *Ipecacuanha* of Brazil. The root is branched, larger and has thinner bark than annulate Ipecac. The roots of other *Hybanthus* species, the root of *Anchietea salutaris* of Brazil and the rhizome of *Viola odorata* have emetic principles.

Bastard Ipecac is the dried root of *Asclepias currassavica* Linné (p. 513).

Indian Ipecac is the dried root of *Tylophora indica* (*asthmatica*).

Goanese Ipecac is the dried root of *Naregamia alata* (Fam. *Meliaceæ*) from the East Indies. The root contains starch, calcium oxalate rosettes, orange-red secretion cells and the alkaloid naregamine. It is strongly emetic.

GAMBIR

Gambir or Pale Catechu (U. S. P. 1905 to 1936; N. F. 1936 to date) is the dried aqueous extract prepared from the leaves and twigs of *Uncaria Gambir* (Hunter) Roxburgh. *Gambir* is the native Malaysian name of the plant.

The plant is a climbing shrub growing in the Malay States and in the East Indies. The natives gather the leaves and twigs and extract them by boiling with water. The aqueous extract is evaporated in tubs and when sufficiently thick is cut into cubes and frequently dried over fires. Most of the drug is produced in Singapore, Bintang and British North Borneo. Gambir is one of the substances known as catechu (Malay *cate,* a tree; *chu,* juice) which were first described about the sixteenth century. The catechu of Barbosa (1514) was probably black catechu. The first account of gambir seems to be that of a Dutch trader in 1790. Its known production in Singapore dates from 1820.

Description.—Usually in more or less porous, dull, irregular cubes, up to 30 mm. in diameter; externally dark reddish gray to light brown; friable; internally weak brown to weak yellowish orange.

Powder.—Color light brown to moderate yellowish brown; inodorous; taste bitterish, very astringent; mostly masses of interlacing acicular crystals up to 30 microns long, which dissolve in water or slowly in chloral T.S.; in the undissolved residue may occur a few leaf fragments, with non-glandular, thick-walled hairs up to 350 microns long; a few simple or compound starch grains, from 5 to 30 microns in diameter; non-living bacteria are usually numerous.

Constituents.—Catechutannic acid, 22 to 50 per cent, resembling the tannin in oak bark, kino and krameria; pyrocatechol, up to 30 per cent; catechin, which crystallizes in silky needles; gambir-fluorescein; catechu red; quercetin; ash, about 3 per cent.

Standards and Tests.—Gambir yields not less than 60 per cent of alcohol-soluble extractive, not less than 70 per cent of water-soluble extractive, and not more than 1 per cent of acid-insoluble ash.

Macerate 1 gm. of powdered gambir with 50 cc. of distilled water for one hour, filter; separate portions of this filtrate give an intense green color with dilute ferric chloride T.S. and no precipitate with cupric sulfate T.S. (*catechutannic acid*).

Extract powdered gambir with alcohol and filter; to the filtrate add sodium hydroxide T.S., and, after shaking, a few cc. of petroleum benzin; upon standing, the benzin layer shows a strong green fluorescence (gambir-fluorescein).

Wet a match stick with an aqueous extract of gambir so diluted as to impart but a slight tint to the wood; dry it, dip it into hydrochloric acid, quickly remove it, and warm it near a flame; a deep purplish red stain is developed (catechin). Compare this test with a similar one using solution of phloroglucin.

Uses and Dose.—Gambir is an astringent. It is also employed in tanning and as a mordant in dyeing. Average dose, 0.5 gm.

Mitchella or Squaw Vine (N. F. 1926 to 1947) is the dried plant of *Mitchella repens* Linné. The plant is a creeping shrub with evergreen leaves, and with stems trailing on the ground, and is common in woods throughout the eastern and central United States. Commercial supplies of the drug come from Virginia and the Carolinas and to some extent from New England. The drug is said to have been employed by the American Indians as a parturient.

The drug is in loosely matted masses consisting of much branched rhizomes with their fine roots together with the stems and leaves; rhizomes light yellowish to dark brown, filiform, with slender fibrous roots; stems quadrangular or flattened, light green, with surface finely striated, bearing opposite leaves; leaves green, coriaceous, rounded-ovate, entire, up to about 2 cm. in length and with a short petiole, upper surface smooth, dark green with prominent midrib and veins, lower surface smooth, light green and somewhat shiny.

The powder is light grayish green; odor faint; taste slightly bitter; numerous raphides of calcium oxalate from 20 to 55 microns in length; greenish fragments of epidermal cells with broadly elliptical stomata, the latter from 20 to 27 microns in length, associated with chlorenchyma cells; tracheæ with spiral or reticulate markings; fragments composed of cortical parenchyma, some of the cells containing raphides of calcium oxalate; starch grains, mostly simple, spheroidal or ellipsoidal and up to about 10 microns in diameter.

Mitchella contains a bitter principle and tannin. The fruit contains a saponin.

Mitchella is used as an astringent, a tonic and a diuretic. Average dose, 2 gm.

Caffea, Coffee Seed or Coffee Bean (U. S. P. 1863 to 1882) is the dried ripe seed of *Coffea arabica* Linné or *Coffea liberica* Hiern, deprived of most of the seed coat.

Caffea Tosta or Roasted Coffee (N. F. 1910 to 1936) is coffee roasted until it is a dark brown color and the characteristic aroma is developed.

The plants are small evergreen trees or shrubs with lanceolate, acuminate, entire, slightly coriaceous, dark green, short-petiolate leaves, which are partly united with the short interpetiolar stipules at the base. The name *Coffea* is from the Turkish *qahveh* or the Arabic *qahuah*, the name of a beverage. The coffee plant is indigenous to Abyssinia and other parts of eastern Africa and is widely cultivated in tropical countries, notably in Java, Sumatra, Ceylon, and Central and South America, particularly Brazil, over 600,000 tons being produced annually in the latter country. The yield of one tree is between 0.5 and 5 kg.

The fruit is a small, spheroidal or ellipsoidal drupe with two locules, each containing one seed or coffee bean. There are two methods of freeing the seeds from the parchment-like endocarp: (*a*) The fruits are allowed to dry and are then broken; in (*b*), which is known as the wet method, the sarcocarp is removed by means of a machine and the two seeds with the parchment-like endocarp are allowed to dry in such a manner as to undergo a fermentation, and after drying, the endocarp is removed. The green seeds are sent into commerce and roasted.

Coffee seed contains from 1 to 2 per cent of caffeine; trigonelline, a non-toxic alkaloid, also found in fenugreek seed; from 3 to 5 per cent of tannin; about 15 per cent of glucose and dextrin; 10 to 13 per cent of a fatty oil consisting chiefly of olein and palmitin; 10 to 13 per cent of proteins; and yields 4 to 7 per cent of total ash, nearly all of which is acid-soluble.

In the roasting of coffee the seeds swell, change their color to dark brown and develop the characteristic odor and flavor. The aroma is due to an oil known as caffeol, a methyl ether of saligenin, and which is developed during the roasting process. The caffeine may be partially sublimed and much of the caffeine of commerce is collected in condensers attached to coffee roasters.

Coffee increases in weight in storage. In paper bags and cartons, the maximum increase in weight is reached in the fall months. During the winter months there is a loss of weight, while during the spring and summer there is little change.

Coffee is required to yield not less than 1 per cent of caffeine, not less than 3 per cent and not more than 5 per cent of total ash, and not less than 10 per cent of fat.

The action of coffee depends upon the caffeine present, which acts on the central nervous system, the kidneys, muscles and heart. Although coffee is mainly a dietetic, it is likewise a stimulant, a nervine and a diuretic. It is of value in the treatment of poisoning by morphine.

Coffee Hulls, Sultan or Sacca Coffee is sometimes substituted for coffee. This consists of the outer layer of the pericarp.

Decaffeinized Coffee is prepared by subliming the caffeine from the coffee beans, yet retaining the pleasant characteristic aroma of coffee. Such preparations have an extensive American market and bring a higher price than the ordinary roasted coffee.

Carob Bean, *Ceratonia siliqua* (Fam. *Leguminosæ*), in a ground condition is not only used as cattle food but has been substituted for coffee. It is distinguished by the sclerenchymatous and crystal fibers, and the cells of the mesocarp, which contain reddish brown, spiral masses that are colored a deep violet or blue on heating with solutions of the alkalis.

COFFEE SUBSTITUTES.—The following have been employed as coffee substitutes and adulterants: chicory; a number of cereals and cereal products; soja beans; lupines; peas; beans; the seed of *Cassia fœtida* under the name of **Mogdad Coffee**; the seed of *Cassia occidentalis;* ground ivory nut (*Phytelephas macrocarpa*), which is distinguished by the thick-walled cells of the endosperm; the ground kernels of the acorns of several species of *Quercus*, which are readily identified by the elongated, more or less swollen, distorted starch grains which have a prominent, elongated cleft in the middle.

Rubia, Madder or Dyer's Madder (U. S. P. 1820 to 1882) is the dried root of *Rubia tinctorium* Linné. The plant is an herbaceous perennial indigenous to the Levant and southern Europe and was formerly cultivated as a dyestuff. The rhizome is creeping, the roots long, cylindrical, wrinkled and brownish red in color. The root contains, before drying, a yellow coloring matter, which upon drying, breaks down into several glucosides and other principles yielding **Alizarin**, a valuable dye for wool and silk. Madder has long had a reputation as a dye, though Alizarin was not discovered until 1826, and since 1868 has been prepared synthetically.

Madder is used in medicine as an emmenagogue. It has been used as an indicator, orange-red with acids and purple to blue with alkalis.

CAPRIFOLIACEÆ, OR HONEYSUCKLE FAMILY

This is a small family of plants numbering 11 genera and about 340 species, mostly indigenous to the northern hemispheres and of great diversity as regards habit, leaves, flowers and fruits. The cork is usually superficial, except in *Sambucus* and *Viburnum,* where it is formed inside the bast layers. Secondary bast fibers are developed in nearly all of the genera, excepting *Viburnum.* The tracheæ usually possess scalariform perforations; the wood fibers have bordered pores; and the medullary rays are mostly narrow. Internal secretory organs are wanting, except in *Sambucus,* where tannin secretory cells occur. The non-glandular hairs are unicellular, stellate, peltate or tufted. The glandular hairs are of two kinds: (*a*) having a uniseriate stalk and a spheroidal or ellipsoidal secreting summit, as in *Lonicera, Sambucus, Triosteum* and *Viburnum;* or (*b*) peltate, having a unicellular stalk and shield of 3 to 7 cells as in *Diervilla.*

VIBURNUM PRUNIFOLIUM

Viburnum Prunifolium or Blackhaw (U. S. P. 1882 to 1926; N. F. 1926 to date) is the dried bark of the root or stem of *Viburnum prunifolium* Linné or of *Viburnum rufidulum* Rafinesque. *Viburnum* is from the ancient Latin, possibly meaning "to bind, to tie or to plait" from the flexibility of the branches of some of the species; *prunifolium* means "leaves resembling those of the plum tree." The plant is a shrub or small tree indigenous to the eastern and central United States. Most of the commercial supplies are gathered in western North Carolina and Tennessee. In 1857 Professor John King recommended it as a uterine tonic. The root-bark is more highly esteemed than the bark of the stem and branches.

Description.—Root Bark: in quills, transversely curved pieces, or irregular oblong chips, 0.5 to 1.5 mm. in thickness; outer surface brown, or, where the cork is removed, brownish red, longitudinally wrinkled and roughened from corky protuberances; inner surface paler, showing light-colored streaks, longitudinally striate; fracture short; periderm brownish red, inner bark with numerous light yellow groups of stone cells.

Stem Bark: In quills or curved pieces up to 6 mm. in thickness; externally grayish, in older bark brownish gray to black, inner surface paler, striated; fracture short but uneven. It should be rossed to the brown middle bark.

Powder.—Light brown to moderate yellowish brown; inodorous, acquiring a valeric acid odor upon aging or exposure to air; taste bitter and astringent; calcium oxalate in rosettes or prisms up to 57 microns in diameter or length; stone cells numerous, up to 260 microns in length, irregular or elongated, often in groups, thick-walled and strongly lignified; bast fibers comparatively few, lignified; starch grains simple or 2- or 3-compound, up to 23 microns in diameter.

Structure.—Root Bark: See Figure 343 and the National Formulary.

Stem Bark: Similar to root bark, except that excessive borke containing cork and stone cells is found in unrossed old bark, and a few pericyclic fibers are found in young bark.

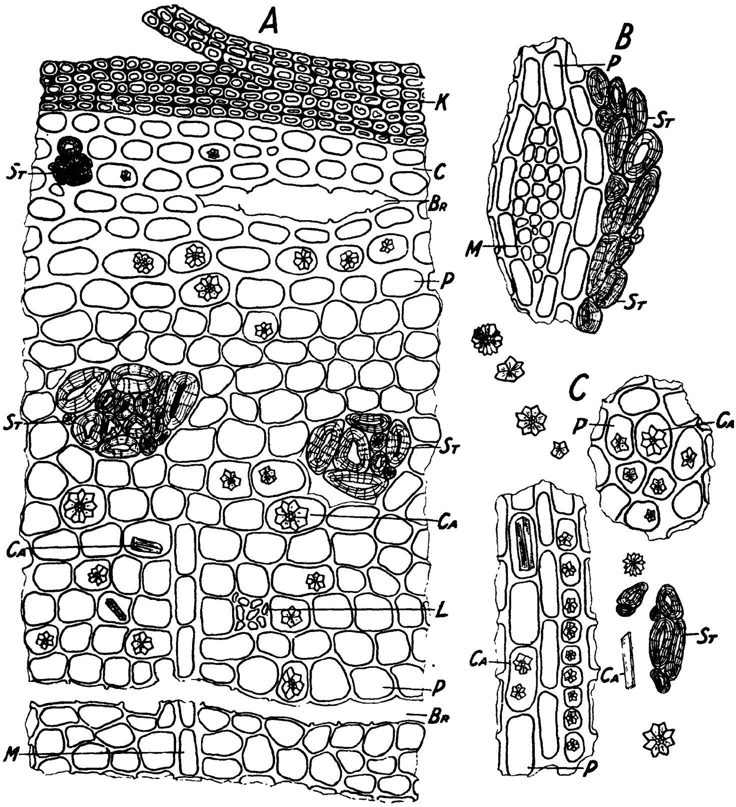


Fig. 343.—*Viburnum prunifolium:* *A*, transverse section of part of the root bark: *K*, several rows of somewhat lignified cork cells, many with a brownish amorphous content; *C*, cortex with parenchyma cells (*P*) the outer rows somewhat collenchymatous; *M*, medullary ray nearly straight and 1 cell wide, though sometimes up to 3 cells wide (*B*); *St*, stone cells in groups, numerous in the middle and inner bark; *Br*, rift between the parenchyma cells which eventually results in the separation of layers of bark; *Ca*, calcium oxalate rosettes or prisms, abundant in parenchyma of phloem and cortex; *L*, groups of sieve cells; *C*, elements of the powder. (By Haase.)

Constituents.—Salicylic alcohol (saligenin), the aglycone of salicin, gives a marked uterine sedative action; a pink, alcohol-soluble polymerization product of saligenin is even more markedly active (J. A. Ph. A. 36: 191, 1947). Also a bitter, somewhat resinous principle, viburnin; valeric (viburnic) acid and other organic acids; resin; tannin; calcium oxalate; ash, about 10 per cent.

Uses and Dose.—Viburnum Prunifolium is an astringent and a tonic. It is also a nervine, a uterine sedative and a diuretic. Average dose, 4 gm.

Adulterants.—The barks of one or more allied species, especially *Viburnum dentatum* and *Viburnum lentago* may sometimes be substituted for the official bark.

VIBURNUM OPULUS

Viburnum Opulus, High-bush Cranberry Bark or True Cramp Bark (U.S.P. 1894 to 1916; N. F. 1916 to date) is the dried bark of *Viburnum opulus* Linné var. *americanum* (Miller) Aiton. *Opulus* means wealth or riches,

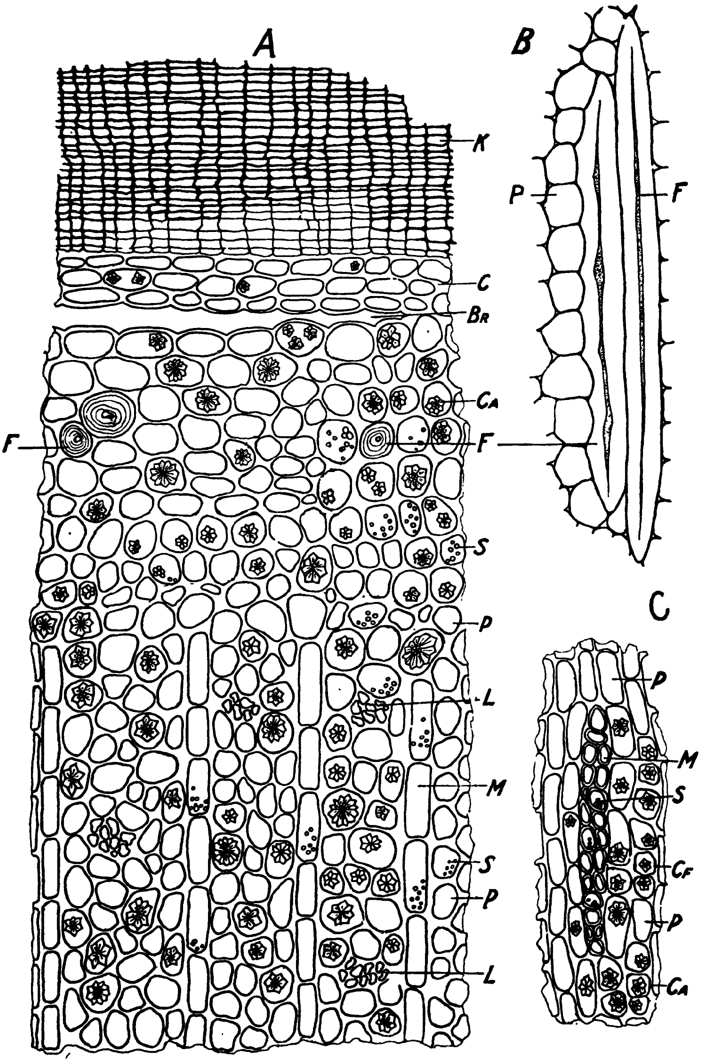


Fig. 344.—*Viburnum opulus: A*, transverse section of the bark: *K*, many layers of thin-walled cork cells in older bark, epidermis in young bark; *C*, parenchyma or chlorenchyma of the cortex containing a greenish yellow amorphous substance, rosette aggregates of calcium oxalate (*Ca*), or starch grains (*S*); *F*, lignified pericyclic fibers; *L*, small groups of sieve; *M*, medullary rays 1 or 2 cells wide; *B*, longitudinal section showing two bast fibers and parenchyma; *C*, tangential section through a medullary ray: letters as above. In older bark secondary phellogens cause exfoliation of the bark and stone cell masses are developed in the phloem. (By Haase.)

in reference to the wealth of foliage. The plant is a shrub with nearly erect branches indigenous to the northern United States and southern Canada. Most of the commercial supplies are gathered from plants growing wild in Minnesota, Michigan and Maine. The bark was employed by the Indians as a diuretic.

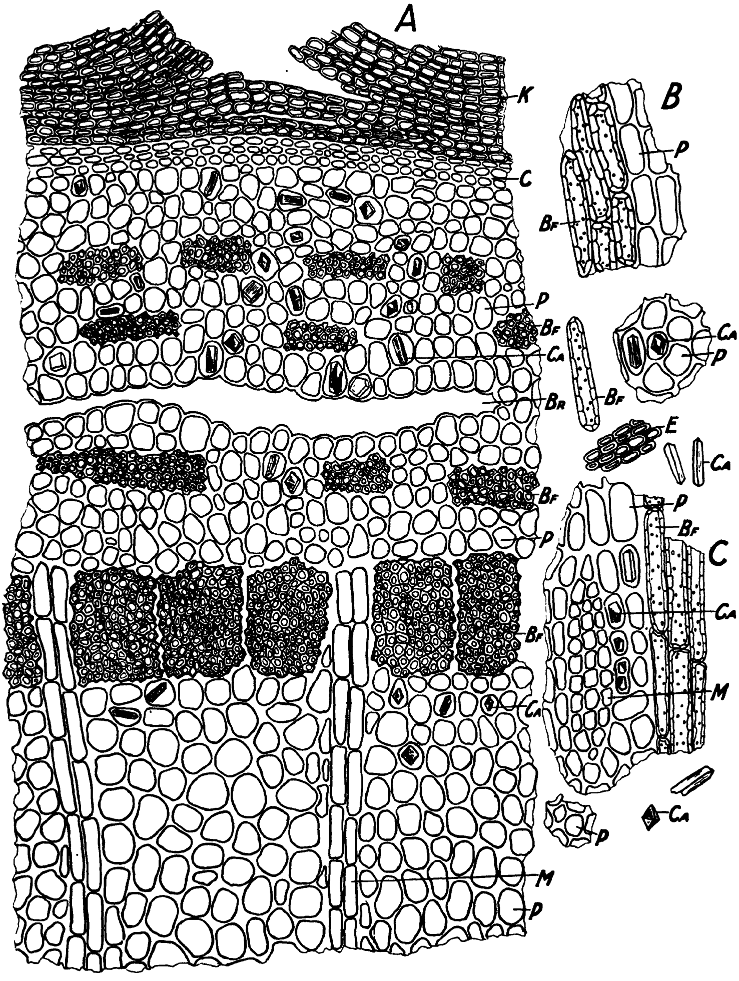


FIG. 345.—*Acer spicatum:* *A*, transverse section of bark showing cork (*K*); a narrow row of thick-walled, tangentially elongated cells (*C*); cortical parenchyma (*P*); calcium oxalate (*Ca*); bast fibers (*Bf*); separation of cells (*Br*); medullary rays (*M*). *B*, Fragments of powdered drug showing short bast fibers (*Bf*); parenchyma (*P*); calcium oxalate (*Ca*) and cork (*E*). *C*, Tangential section, showing medullary rays (*M*); calcium oxalate (*Ca*); parenchyma (*P*); bast fibers (*Bf*). (Drawing by Haase.)

DESCRIPTION.—In strips, or occasionally in quills or chip-like fragments, the bark up to 3 mm. in thickness; outer surface of the thinner pieces purple to greenish brown or greenish yellow, sometimes with crooked longitudinal wrinkles and a few, small brown lenticels; the thicker pieces from light gray and grayish brown to grayish black or black (where abraded, greenish to brown) and finely fissured or scaly; inner surface from greenish yellow to rusty brown, with short oblique or irregular striæ, except where the wood adheres; fracture finely fibrous in thinner bark to short and weak in thicker bark; the fractured surface with a brownish outer bark, a greenish phelloderm, and pale brown to yellowish inner bark.

STRUCTURE.—See Figure 344 and the National Formulary.

POWDER.—Pale brown to weak yellowish orange; odor slight, but characteristic, becoming like valeric acid upon aging or, upon trituration with phosphoric acid; taste somewhat astringent and decidedly bitter; parenchyma fragments bearing starch and rosette crystals of calcium oxalate, the latter up to 42 microns in diameter, and a yellowish brown amorphous substance; cork fragments with polygonal, tabular cells, occasionally with lignified walls; stone cells variable in shape, up to 124 microns long and 35 microns thick; occasional primary bast fibers with thick, lamellated somewhat lignified walls; starch grains mostly simple, seldom exceeding 6 microns in diameter.

CONSTITUENTS.—The constituents resemble those of Viburnum Prunifolium.

USES AND DOSE.—Viburnum Opulus is an antispasmodic and a sedative. Average dose, 2 gm.

ADULTERANTS.—The bark of Mountain Maple (*Acer spicatum*) has been substituted for Viburnum Opulus. The former is distinguished (Fig. 345) by the numerous rhombohedral crystals of calcium oxalate and large groups of bast fibers.

SAMBUCUS

Sambucus or Elder Flowers (U. S. P. 1831 to 1905; N. F. 1916 to 1947) is the air-dried flower of *Sambucus canadensis* Linné or of *Sambucus nigra* Linné. *Sambucus* is from the Latin *samburca*, meaning a stringed instrument made from elder-wood; *canadensis* refers to the habitat and *nigra* is Latin for black.

The American Elder (*S. canadensis*) is a large shrub growing in rich moist soil throughout the eastern and central United States. The European Elder (*S. nigra*) of Europe, western Asia and western Africa may attain a height of 30 feet. The plant has odd-pinnate leaves, small white flowers, which are borne in flat cymes, and deep purple or nearly black drupes. The latter are edible and sometimes used in making a wine. The flowers are gathered in early summer during the dry and hot weather, carefully dried and preserved.

Most of the commercial supply is imported from Europe through Hamburg, Budapest and Trieste.

The flower is usually shriveled, from 1 to 3 mm. in diameter; corolla, white when fresh, when dry weak yellowish orange to moderate yellow, urn-shaped and possessing 5 spreading lobes; stamens 5, inserted at the base of the corolla; ovary 3-locular and containing an ovule in each loculus; pollen grains numerous, spheroidal, up to 25 microns in diameter, nearly smooth and having 3 pores; odor aromatic; taste mucilaginous, slightly aromatic and bitter.

Sambucus contains considerable mucilage, a little tannin and a semisolid, yellowish volatile oil with the odor of elder blossoms, which becomes more prominent as the oil is diluted. Total ash about 6.6 per cent; acid-insoluble ash 0.6 per cent.

Sambucus is used principally for distilling **Elder Flower Water,** as a fragrant perfume and flavor. A sterilized clear infusion of elder flowers is used in collyria; the mucilage is not precipitated with alcohol; the drug is a mild stimulant, carminative and diaphoretic. Average dose, 4 gm.

Sambuci Baccæ or Elder Berries (U. S. P. 1820 to 1831) are the fruit of *Sambucus canadensis* Linné. The juice expressed from the berries contains mucilage, sugar and malic acid. It has long been used for making **Elder Berry Wine.** The freshly expressed, clarified juice, evaporated to a soft extract, has been recognized in European pharmacopœias as the base of a refrigerant, diuretic drink.

Elder Bark and Elder Leaves have been used as a purgative and diuretic, especially in dropsy.

Triosteum or Fever Root (U. S. P. 1820 to 1882) is the root of *Triosteum perfoliatum* Linné. The plant is a perennial herb up to 1.3 meters high, indigenous to rich woodlands in the United States. The rhizome is horizontal, up to 25 cm. long and 2 cm. thick; the roots are numerous, up to 25 cm. long and yellowish brown in color. The fresh root is nauseous and bitter in taste, and in doses of 1 to 2 gm. is an active purgative and emetic.

VALERIANACEÆ, OR VALERIAN FAMILY

This is a family of 10 genera and about 350 species of herbs mostly indigenous to the northern hemispheres. The leaves are opposite; the flowers are usually small, the ovary being inferior, and the fruits are dry and indehiscent. The secretion cells have suberized walls and contain a volatile oil. In the rhizome and roots of *Valerian* the volatile oil is developed in the subepidermal layer. The walls of the tracheæ and wood fibers are marked by simple pores, except in the primary xylem where the tracheæ possess scalariform perforations. The non-glandular hairs are usually unicellular. The glandular hairs are small, having either a unicellular or a multicellular stalk and a multicellular summit. Calcium oxalate is wanting.

VALERIAN

Valerian (U. S. P. 1820 to 1942; N. F. 1942 to date) consists of the dried rhizome and roots of *Valeriana officinalis* Linné. Valerianus, emperor of Rome, A.D. 253 to 260, first used the plant in medicine, hence the plant name given in the ninth century A.D. The plant is a perennial herb indigenous to Europe and Asia and cultivated in Holland, Germany, England and the United States, being more or less naturalized in this country as far south as New York and New Jersey. The rhizome is collected in autumn, cut into longitudinal slices and dried by artificial heat. There are several commercial varieties and it is said that some of the drug is derived from *Valeriana sylvatica.* Most of the commercial supply comes from Belgium and Holland. During medieval days valerian was used in cookery for its *delightful* flavor, and in the sixteenth century was accepted as a perfume, as it is employed in the Orient today.

Description.—Rhizome upright, slightly ellipsoidal, more or less truncate at both ends, from 2 to 4 cm. in length, and 1 to 2 cm. in diameter, usually cut longitudinally into 2 or 4 pieces; externally weak brown to moderate yellowish brown, the upper portion having circular stem and leaf-scars, the sides sometimes with a short branch or stolon from 5 to 8 cm. in length and with numerous roots and few root-scars; fracture short, horny; internally light brown.

Roots 3 to 10 cm. in length, 0.5 to 1 mm. in diameter, longitudinally wrinkled and brittle.

Structure.—Root: epidermis of papillose cells, some being modified to root-hairs; subepidermal layer containing suberized secretion cells usually containing numerous small oil globules and occasionally small prismatic crystals; cortical parenchyma filled with starch; endodermis of thin-walled cells surrounding a pericambium; central cylinder with a radial fibrovascular bundle; tracheæ with simple and bordered pores. Older roots show a large pith of starch-bearing parenchyma, a secondary thickening in the fibrovascular bundles and a periderm of a few layers of cells. Sections of the rhizome show a thin periderm, a cortical parenchyma having scattered fibrovascular bundles, a layer of altered cells of the endodermis, numerous more or less twisted, collateral, fibrovascular bundles and a large pith.

POWDER.—Color weak brown to moderate yellowish brown; odor of valeric acid, becoming stronger upon aging; taste sweetish, camphoraceous and somewhat bitter; starch grains numerous, from 3 to 20 microns in diameter, spheroidal, plano-convex, polyhedral, 2- to 4-compound and each usually with a central cleft; tracheæ having simple and bordered pores or scalariform and reticulate thickenings, accompanied by narrow sclerenchymatous fibers, the walls of the latter being thin, porous and strongly lignified; occasional fragments of epidermis with root-hairs and fragments of cork.

CONSTITUENTS.—A volatile oil, 0.5 to 2 per cent, composed of bornyl valerate (9.5 per cent), bornyl formate, bornyl acetate, bornyl butyrate, borneol, pinene, camphene, and a sesquiterpene; an alkaloid, 0.015 per cent, a glucoside, a resin (all three physiologically active); free formic and acetic acids and malates; tannin; saccharose; starch. Total ash, 4.3 per cent; acid-insoluble ash, 0.5 per cent. The valerian odor is due to isovaleric acid, formed from bornyl acetate by an oxydase during the drying of the drug.

USES AND DOSE.—Valerian is used as an antispasmodic and a nervine. Average dose, 0.75 gm.

Oleum Valerianæ or Oil of Valerian (U. S. P. 1851 to 1894) is the volatile oil distilled from the rhizome and root of *Valeriana officinalis* Linné. The freshly gathered root is crushed or ground and distilled with water, the yield being larger from plants grown in dry soils. When recently prepared, the oil is yellowish or greenish, of a mild odor and a neutral reaction. On exposure to air it becomes brownish, of a strong odor and with an acid reaction. It is readily soluble in alcohol. Its constituents are given under Valerian. It is used as a sedative for hysteria. Dose, 0.05 to 0.1 cc.

Acidum Valerianicum or Valeric Acid (U. S. P. 1863 to 1882), $CH_3.CH_2.CH_2.CH_2.COOH$, is formed by oxidation in valerian and in other plants, but is usually prepared synthetically by oxidizing amylic alcohol. It is a colorless liquid with a disagreeable odor, and is soluble in alcohol. It readily forms crystalline salts with alkalis.

Acid Ammonium Valerate (N. F. 1926 to date) is a nerve sedative, useful in nervous headache, insomnia, hysteria, neuralgia, etc.

ADULTERANTS AND SUBSTITUTES.—The most dangerous admixture that has been reported is veratrum, which is readily distinguished. *Cypripedium macranthum* (Fam. *Orchidaceæ*), of Germany has been used as a substitute for valerian.

ALLIED PLANTS.—**Kesso Root Oil** is obtained from **Japanese Valerian** (*Valeriana angustifolia*). The constituents are similar to those of the volatile oil in valerian, but it contains in addition kessyl acetate and kessyl alcohol. It has an unpleasant flavor and gives a different taste to the tincture. **Mexican Valerian,** derived from *V. mexicana,* yields an oil containing about 89 per cent of isovaleric acid. **Indian Valerian** (*Valeriana wallichii*) is as valuable as English-grown valerian and more agreeable to the taste.

The small rhizomes of *Valeriana celtica,* a plant growing in the Styrian Alps, yield a volatile oil with an odor resembling that of anthemis and patchouly.

CUCURBITACEÆ, OR PUMPKIN FAMILY

This is a family of about 100 genera and 800 species of mostly tropical, more or less prostrate climbing vines. The leaves are usually palmately lobed; the stamens are more or less united either by their filaments or tortuous anthers, and the fruits are fleshy and indehiscent. The fibrovascular bundles are bicollateral and always separated by broad strands of parenchyma. In the herbaceous stems there is always a closed ring of sclerenchyma in the cortex and the fibrovascular bundles are arranged in 2 interrupted circles. In the fleshy perennial roots and shrub-like stems, showing a secondary growth, broad medullary rays are developed. Furthermore, there may also occur from 5 to 7 concentric rings of bundles, the sclerenchyma of the cortex being reduced to isolated groups of sclerenchymatous fibers. The phloem is developed in other parts of the plant than in the fibrovascular bundles. The tracheæ are wide and the walls possess simple pores. The non-glandular hairs are unicellular or uniseriate and the cuticle is sometimes spinose, as the hairs on the leaves of *Bryonia, Cucumis, Cucurbita* and *Ecballium.* The glandular hairs have a short uniseriate stalk and a 4-celled summit. Cystoliths and cystolith-like structures are of common occurrence in a number of genera. Calcium oxalate is occasionally secreted in the form of solitary crystals.

COLOCYNTH

Colocynth, Colocynth Pulp or Bitter Apple (U. S. P. 1820 to 1936; N. F. 1936 to date) is the dried pulp of the unripe but full-grown fruit of *Citrullus Colocynthis* (Linné) Schrader.

Citrullus is the diminutive of *citrus* in allusion to the resemblance of the fruit to the orange; *Colocynthis* is from the Greek meaning a gourd or pumpkin. The plant is a perennial herbaceous vine, indigenous to warm, dry regions of Africa and Asia, and cultivated occasionally. The gathered fruit are peeled to remove the epicarp and quickly dried in the sun or artificially. Cultivated fruits are larger, but the drug from them is inferior. Commercial supplies are largely from Turkey, Spain and the Sudan, the finest grade being from Turkey. The seed are to be removed from the pulp before it is used.

Colocynth was well known to the Greeks and Romans and is mentioned by both Dioscorides and Pliny. The drug was known to the Arabian physicians and was cultivated in Cyprus and Spain during the Middle Ages.

Description.—Berry nearly globular, 4 to 10 cm. in diameter (Fig. 346); peeled; internally, with 3 longitudinal, somewhat elliptical fissures, 8 to 14 mm. in width; seed numerous, ovoid, compressed, light yellow to brown and borne on the parietal placentas; the pulp is light in weight, spongy, easily broken, light yellowish orange to pale yellow.

Structure.—See Figure 347.

Powder.—Weak yellowish orange to yellowish gray; odor slight; taste intensely bitter; consisting chiefly of thin-walled, porous parenchyma cells, and rarely small tracheæ accompanied by irregular, tubular laticiferous vessels; very few or no lignified tissues, globules of fixed oil or aleurone tissues. The powdered drug with seed present contains numerous oil globules, aleurone grains and thick-walled, lignified stone cells (see Fig. 347).

Constituents.—An amorphous glucoside in very small quantity, and an ether-chloroform-soluble resin probably represent the powerful activity of the drug; the inactive *a*-elaterin is present, but apparently none of the physiologically active *b*-elaterin; "colocynthin" and "colocynthitin" are indefinite mixtures; "citrullol" is a phytosterol glucoside; considerable pectin and albuminoids are present. The seed contain about 15 per cent of a fixed oil. The pulp alone yields, on an average, 9.9 per cent of natural ash, all of which is soluble in diluted hydrochloric acid.

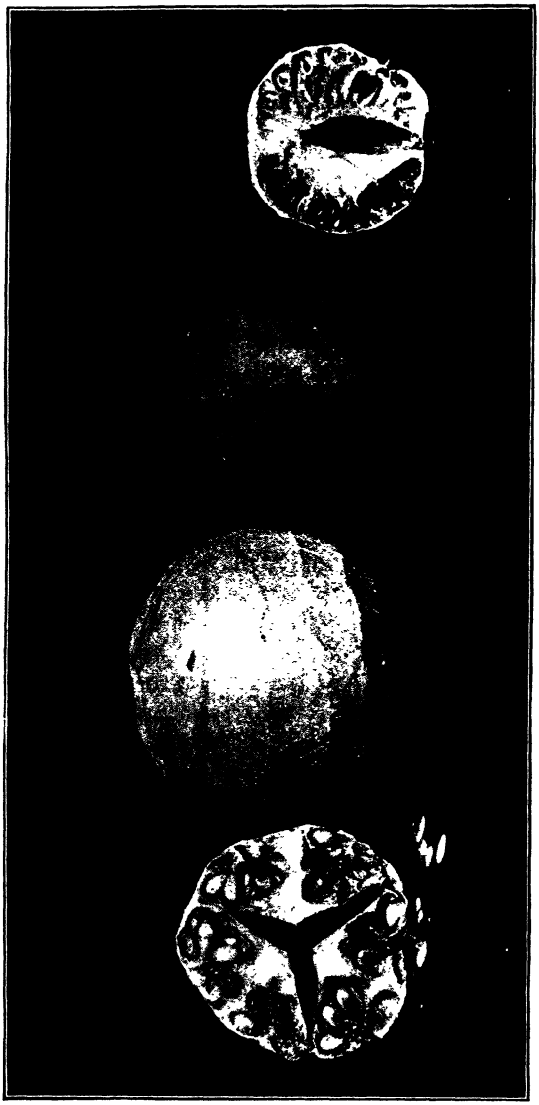


Fig. 346.—Colocynth fruits: Beginning at the left is seen a transverse section, fruit with epicarp removed, fruit with epicarp present, and longitudinal section.

Standards and Tests.—Colocynth contains not more than 5 per cent of seed and not more than 2 per cent of epicarp and yields not more than 2 per cent of extractive with purified petroleum benzin and not more than 4 per cent of acid-insoluble ash.

Characteristic stone cells are few or absent in powdered colocynth (*epicarp and seed*). Aleurone grains and globules of fixed oil are few or absent (*seed*).

USES AND DOSE.—Colocynth is a drastic purgative or hydragogue cathartic. Average dose, 125 mg. "Colocynthin," 5 to 10 mg.

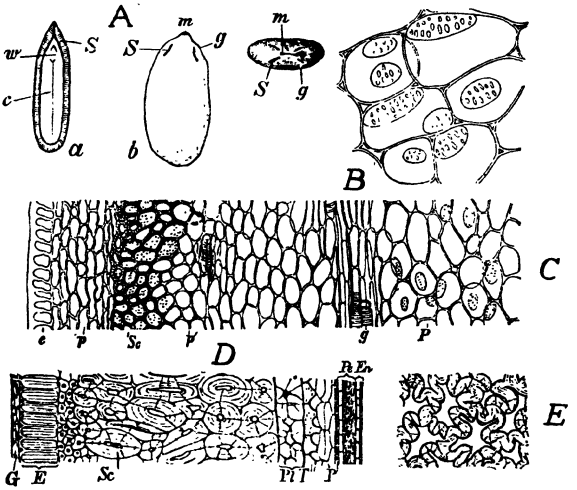


FIG. 347.—*Citrullus colocynthis:* *A*, seed: *a*, in longitudinal section, and *b*, surface view; *S*, deep clefts or fissures; *m*, micropyle; *g*, hilum; *w*, radicle; *c*, cotyledons. *B*, Parenchyma cells of ripe fruit showing simple pores; the walls are colored blue with zinc chloriodide. *C*, Longitudinal section of wall of pericarp of ripe fruit showing *e*, epidermis; *p*, parenchyma; *Sc*, sclerotic cells which gradually pass into a thick-walled parenchyma consisting of small cells (*p'*); *g*, spiral vessels; *P*, isodiametric, porous parenchyma cells, containing air and of which the fruit for the most part consists. *D*, Cross-section of seed coat showing *G*, an outer layer which is more or less easily separable from the rest of the seed and the walls of which are somewhat mucilaginous; *E*, epidermis of palisade-like cells; *Sc*, sclerotic cells; *Pl*, a layer of tabular cells with undulate walls; *T*, a layer of small, somewhat branching cells, the walls of which are not strongly thickened and either porous or reticulate; *P*, several layers of parenchyma and the collapsed epidermis; *Pe*, perisperm; *En*, endosperm; *E*, tangential section of tabular sclerotic cells of seed coat shown in *Pl* in Fig. *D*. (After Meyer.)

BRYONIA

Bryonia or Bryony (U. S. P. 1882 to 1905; N. F. 1916 to date) is the dried root of *Bryonia alba* Linné or of *Bryonia dioica*, Jacquin.

Bryonia, the Greek name, meaning to swell, alludes to the annual growth of the tuber; *dioica* means two households, alluding to the polygamous nature of the flowers; *alba*, Latin, means white, referring to the flowers. The plants are perennial vines indigenous to central and southern Europe. *B. alba* produces black berries and *B. dioica* red berries. The root is gathered in the summer or fall, cut transversely into pieces and used either in the fresh or dried condition.

DESCRIPTION.—In nearly circular disks, up to 10 cm. in diameter and 15 mm.. thick; the edges are weak yellowish orange and very roughly wrinkled; the cut surface, nearly white or yellowish white, shows a cortex about 2 mm. in width, a very broad radiate xylem, made up of concentric zones of bicollateral fibrovascular bundles.

Powder.—Weak yellowish orange to weak yellow; odor faint but characteristic; taste bitter and nauseous; fragments of yellowish cork with thin-walled elongated cells; elongated, starch-bearing parenchyma cells of bark and medullary rays with cylindrical secretion cells containing a granular content; numerous simple or compound, rounded starch grains, up to 25 microns in diameter and usually with a central cleft; tracheal fragments with reticulate or simple pores.

Constituents.—Bryonin, a yellow, amorphous, bitter, toxic, probably impure, strongly cathartic glucoside; Bryonidin, a colored, amorphous, bitter, toxic, readily soluble, probably impure glucoside which paralyzes the central nervous system; Bryonol, a phytosterol glucoside; Bryonicine, a white, amorphous alkaloid, insoluble in water, but forming soluble salts; a small amount of a volatile oil; a sugar; a mixture of fatty acids; and an enzyme which hydrolyzes bryonin to a resin and dextrose, and also effects the hydrolysis of amygdalin and salicin. Total ash, 5.45 per cent; acid-insoluble ash, 0.6 per cent.

Uses and Dose.—Bryonia is a hydragogue cathartic. Average dose, 1 gm.

Elaterium (U. S. P. 1820 to 1882) is the dried precipitated residue from the fresh juice of the full-grown but unripe fruit of *Ecballium Elaterium* (Linné) A. Richard.

Elaterinum or Elaterin (U. S. P. 1882 to 1936) is a substance extracted from Elaterium.

The plant, known as Squirting Cucumber, is a decumbent, perennial herb indigenous to the Mediterranean region and cultivated in central Europe and England. The fruit is ovoid, fleshy, about 4 cm. in length, covered with numerous, uniseriate glandular hairs and when unripe, of a pale green color. When ripe, the fruit separates suddenly from the stalk, the juice with the seed being forcibly ejected from the aperture left by the detached peduncle.

To obtain the juice, the unripe fruits are sliced longitudinally, gently pressed, then rinsed with cold water. The juice is strained through cloth, allowed to stand two hours, then decanted and re-precipitated. The precipitate is collected on filter paper, and pressed between warm, dry absorbent bricks until dry. Forty pounds of fresh fruit yields from 15 to 30 gm. of dry Elaterium.

It usually occurs in rectangular pieces, from 3 to 4 cm. in length and about 5 mm. in thickness. When fresh, it is of a greenish brown color, changing to a light grayish brown on keeping. It has a granular fracture, a somewhat aromatic odor and an acrid, bitter taste. It contains up to 40 per cent of elaterin; 17 per cent of a resin; 6 per cent of starch.

Elaterin is a white, crystalline powder (*very poisonous*) of very bitter taste, insoluble in cold water, but soluble in hot alcohol, about 1 to 100; it is extracted from elaterium with hot alcohol, the alcohol partially evaporated, then the drug is precipitated in cold water and purified by recrystallization from ether. It contains *b*-elaterin in small quantity, dextrorotatory, and powerfully purgative; *a*-elaterin, up to 80 per cent, levorotatory and completely devoid of purgative action; some other inert material.

Both drugs are drastic purgatives. Average dose of elaterium, 10 to 30 mg.; of elaterin, 2 to 6 mg.

Pepo or Pumpkin Seed (U. S. P. 1863 to 1936) is the dried, ripe seed of cultivated varieties of *Cucurbita Pepo* Linné, a procumbent herb native of tropical America and long cultivated in tropical and temperate zones. The seed are anatropous, broadly elliptical, flattened, 15 to 25 mm. in length, and 2 to 3 mm. in thickness; externally nearly white or light yellow, very smooth or somewhat rough from adhering fruit pulp, marked by a shallow groove parallel to and within 1 mm. of the margin; seed coat of 2 distinct layers, the outer white and coriaceous and the inner dark green and membranaceous; embryo white, straight, with a small hypocotyl and 2 plano-convex cotyledons; slightly odorous when contused; taste bland and oily.

The outer epidermal layers consist of palisade-like cells, the outer walls usually being torn off so that it appears as though the seed were covered with very long hairs; small, starch grains may be present in these cells; a subepidermal layer consisting of 5 to 12 rows of cells having slightly thickened, lignified and porous walls; a layer of strongly lignified stone cells, elliptical in outline, from 45 to 100 microns long; a single layer of small cells resembling those of the subepidermal layer; several rows of spongy parenchyma cells, with characteristic reticulate markings and separated from each other by large intercellular spaces; several layers of parenchyma cells, the inner layer being more or less collapsed and having on the inner portion a single epidermal layer, the cells having rather thick walls; the perisperm cells are usually more or less collapsed; the endosperm consists of a single layer of cells filled with small aleurone grains; the cotyledons consist of thin-walled, isodiametric, elongated, or palisade-like cells containing a fixed oil and numerous small aleurone grains.

Pepo contains fixed oil about 40 per cent; starch about 30 per cent; proteins; an acrid resin. Total ash about 4.55 per cent, mostly acid-soluble.

Pepo is an anthelmintic and a tænifuge. The seeds of other species of *Cucurbita* are also used in medicine; in Italy *C. maxima* (Winter Squash) and in the West Indies *C. occidentalis* are the sources of the drug.

The seed of Cucumber (*Cucumis sativus*), Muskmelon (*Cucumis melo*) and Lagenaria (*Cucurbita lagenaria*) are also occasionally used medicinally as is pumpkin seed. Watermelon seed (*Citrullus vulgaris*) contains a fixed oil and a resin, which consists in part of a crystalline compound, cucurbitol.

CAMPANULACEÆ, OR BLUEBELL FAMILY

This is a family of 61 genera and about 1500 species, which are widely distributed, those occurring in temperate regions being perennial herbs, while those of the tropics include shrubs and trees. The leaves are alternate; the flowers are regular and have either bell-shaped or somewhat bilabiate corollas; the fruits are either capsules or berries. A very striking characteristic of the family is the occurrence of inulin in place of starch. Laticiferous tubes are abundantly developed in *Lobelia,* even occurring in the pith, the branches penetrating the tissues of the xylem and uniting with the tubes in the cortex. They are also found in other genera. The leaf-teeth are usually terminated by glands, and in close proximity to them on the upper surface are large water pores. The non-glandular hairs are unicellular, being occasionally silicified. Calcium oxalate and glandular hairs are wanting.

LOBELIA

Lobelia or Indian Tobacco (U. S. P. 1820 to 1936; N. F. 1936 to date) consists of the dried leaves and tops of *Lobelia inflata* Linné. *Lobelia* was named in honor of Matthias de L'Obel, a Flemish botanist; (1538–1616); *inflata* is descriptive of the fruit, which is hollow and distended. The plant is an annual herb (Fig. 348) indigenous to the eastern and central United States and Canada.

Commercial supplies come from cultivated plants in Massachusetts, New York and Michigan. It should be collected after a portion of the capsules have become inflated, and carefully dried and preserved. Lobelia was employed by the Indians when necessity required, as a substitute for tobacco. Its emetic properties were first observed by Cutter in 1785, and Thompson introduced it into medicine in 1807.

Description and Structure.—See Figure 348 and the National Formulary.

Powder.—Color dusty yellow to weak greenish yellow; odor slightly irritating; taste strongly acrid; it contains conical non-glandular hairs up to 1.11 mm.

in length; fragments of stem with tracheæ showing annular or spiral thickenings or simple pores associated with narrow wood fibers, the walls of the latter being rather thin, more or less lignified and porous; fragments of epidermis of leaf with elliptical stomata, up to 35 microns in length and usually with 3 or 4

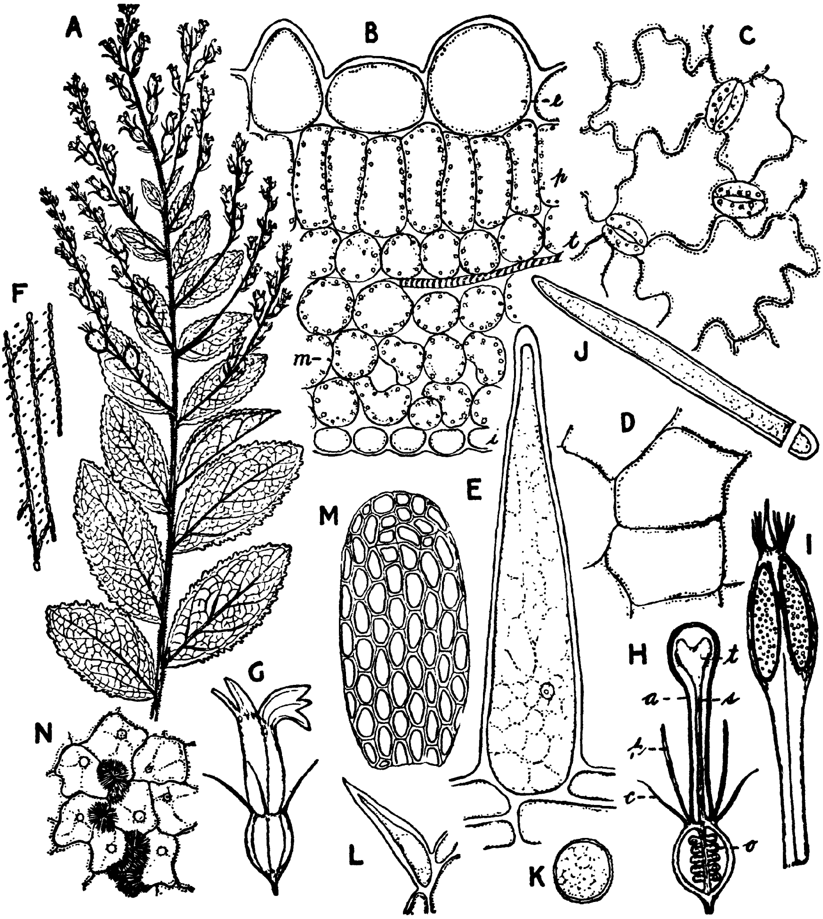


FIG. 348.—Indian tobacco (*Lobelia inflata*): *A*, upper portion of shoot showing the dentate-denticulate leaves and the inflated capsules which develop soon after fertilization; *B*, transverse section of leaf showing the large epidermal cells (*e*), palisade cells (*p*), tracheæ (*t*), loose parenchyma (*m*) and lower epidermis (*i*); *C*, surface section of lower epidermis showing 3 elliptical stomata; *D*, surface section of upper epidermis; *E*, one of the hairs which are found on the stems and leaves; *F*, wood fibers of the stem; *G*, a flower; *H*, longitudinal section of flower showing the ovary with ovules (*o*), style (*s*), hairy bifid stigma (*t*), united stamens (*a*), corolla (*p*) and calyx (*c*); *I*, longitudinal section of stamen showing the hairy summit; *J*, hair from stamen; *K*, pollen grain; *L*, hair from calyx; *M*, seed with reticulate seed coat; *N*, upper epidermis of corolla showing spherite crystals of a carbohydrate.

neighbor cells; pollen grains nearly spheroidal, 20 to 30 microns in diameter; seeds strongly reticulate, the seed coat composed of yellowish brown, polygonal cells having thick walls; fragments of branched laticiferous ducts having a granular content.

CONSTITUENTS.—The alkaloids lobeline, lobelanidine, and lobelanine; a non-acrid but pungent volatile oil; a colorless, tasteless, crystalline neutral principle, inflatin; lobelic acid; waxy, fatty, resinous and gummy matters.

Lobeline or *l*-Lobeline (to distinguish it from a mixture of the lobelia alkaloids also known as lobeline) occurs in colorless crystals very slightly soluble in water, but readily soluble in hot alcohol.

Lobeline Hydrochloride is soluble in water, readily so in alcohol, and very soluble in chloroform. It is used as a prompt and powerful respiratory stimulant. Dose: subcutaneously, 15 mg.; intravenously, 5 to 10 mg.

STANDARDS.—Lobelia contains not more than 10 per cent of its stems over 2 mm. in diameter and not more than 4 per cent of other foreign organic matter, and yields not more than 5 per cent of acid-insoluble ash.

USES AND DOSE.—Lobelia is an expectorant and an emetic. Average dose, 0.1 gm.

Lobelia Seed are very small, brown, and resemble tobacco seed. They contain 30 per cent of fixed oil and lobeline. The oil, when pure, is bland, rapid-drying and resembles linseed oil.

Commercial **Lobelia Oil** is obtained by extracting the herb with ether (which is then recovered) leaving a greenish, acrid oil containing the lobelia alkaloids.

ADULTERANT.—The seed of mullein (*Verbascum thapsus*) are commonly used as an adulterant of lobelia seed, but are distinguished from them by not being reticulate.

ALLIED PLANTS.—Red lobelia or cardinal flower, *Lobelia cardinalis*, and Blue lobelia, *L. syphilitica*, as well as a large number of other species of *Lobelia*, are used to some extent in medicine. *Lobelia nicotianæfolia* of India and *Delissea acuminata* of the Hawaiian Islands have properties similar to *Lobelia inflata*.

COMPOSITÆ, OR COMPOSITE FAMILY

This is the largest family of phanerogamous plants, comprising about 1000 genera and 23,000 species, which are very widely distributed. They are distinguished from all other plants in that the inflorescence is a head or capitulum, consisting of one or two kinds of flowers, arranged on a common torus and subtended by a number of bracts, forming an involucre. The flowers are epigynous and the fruit is an achene, usually surmounted by the persistent calyx, which consists of hairs, bristles, teeth or scales, which are known collectively as the pappus.

The individual flowers are called florets and may be hermaphrodite, pistillate, monœcious, diœcious or neutral. Depending upon the shape of the corolla, two kinds of flowers are recognized, one in which the corolla forms a tube, which is 5-lobed or 5-cleft, known as tubular flowers; and one in which the petals are united into a short tube, with an upper part that forms a large, strap-shaped, usually 5-toothed limb, known as ligulate flowers.

In some of the plants of the *Compositæ* the head consists of ligulate flowers only, as in dandelion, chicory and lettuce; but in the larger number of species the head is composed of both tubular and ligulate flowers or of tubular flowers alone. When the head consists only of tubular flowers it is called discoid, but when ligulate flowers are also present it is called radiate. When the heads are radiate, as in the common daisy, the tubular flowers are spoken of as disk-flowers, and the ligulate flowers as ray-flowers. The disk-flowers are usually perfect, while the ray-flowers are pistillate or neutral (without either stamens or pistils). Usually the stamens in the tubular flowers are syngenesious and the marginal or ray-flowers are distinctly ligulate. However, in a small group represented by the ragweed, the anthers are not united, though close together, and the corolla in the marginal flowers is reduced to a short tube or ring.

The *Compositæ* are characterized by having inulin in the cell-sap of the parenchyma cells, especially in the underground organs. Inulin usually occurs in solution, but may be caused to separate by immersing the parts in alcohol, to form sphærite aggregates, which are not enclosed by a distinct membrane. Laticiferous vessels are common to all of the plants of the *Cichorieæ*. These vessels occur either on the inner face of the strands of phloem or are distributed in the pericycle of the stems. Schizogenous resin canals are distributed among the parenchyma cells of the primary cortex and pith of a large number of the genera. Secretory cavities and elongated secretory cells are also found in a number of genera. The non-glandular hairs are usually uniseriate. The glandular hairs are widely distributed and polymorphic. The stomata are usually surrounded by 3 or more epidermal cells. Calcium oxalate is secreted occasionally in the form of small needles or octahedra and very rarely in the form of rhombohedra or rosettes.

ARNICA

Arnica or Leopard's Bane (plant) (U. S. P. 1820 to 1851); **Arnica or Arnica Flowers** (U. S. P. 1851 to 1926; N. F. 1926 to date); **Arnicæ Radix or Arnica Root** (U. S. P. 1882 to 1905) are the dried plant, the dried flower-head, and the dried rhizome and roots, respectively, of *Arnica montana* Linné. In 1947 arnica became: "The dried flower-head of *Arnica Montana* Linné, known in commerce as European Arnica, or of *Arnica fulgens* Pursh, *Arnica sororia* Greene, and *Arnica cordifolia* Hooker, known in commerce as American Arnica."

These perennial herbs are indigenous to cold mountainous regions; *A. montana* in central Europe and all of these species in northwestern United States and southwestern Canada.

Formerly the commercial drug came from central Europe but during World War II, when European imports ceased, Montana arnica met the need and is now considered equal to, if not superior to, the European drug. Arnica was used in Europe as early as the Sixteenth century. About 1680 it was enthusiastically received as a new remedy for fevers, but soon fell into disuse.

Description and Structure.—See Figure 349 and the National Formulary.

Constituents.—A bitter crystalline principle, arnicin, about 4 per cent; a butyraceous volatile oil, 0.5 to 1 per cent in Arnica Root; resins; butyric, formic and angelic acids. Total ash, 7.65 per cent; acid-insoluble ash, 0.65 per cent.

Adulterants.—Arnica flowers are not infrequently adulterated with the flowers of various other *Compositæ*, or even entirely substituted by them; of these may be mentioned the flowers of *Calendula officinalis* (see Calendula); species of *Inula*, the achenes of which are glabrous; and *Tragopogon pratensis*, the ligulate florets of which are 5-toothed at the apex. The flowers of *Inula britannica* are smaller, the ligulate flowers are 4-veined, the receptacle is smooth and the achene is about 1 mm. in length.

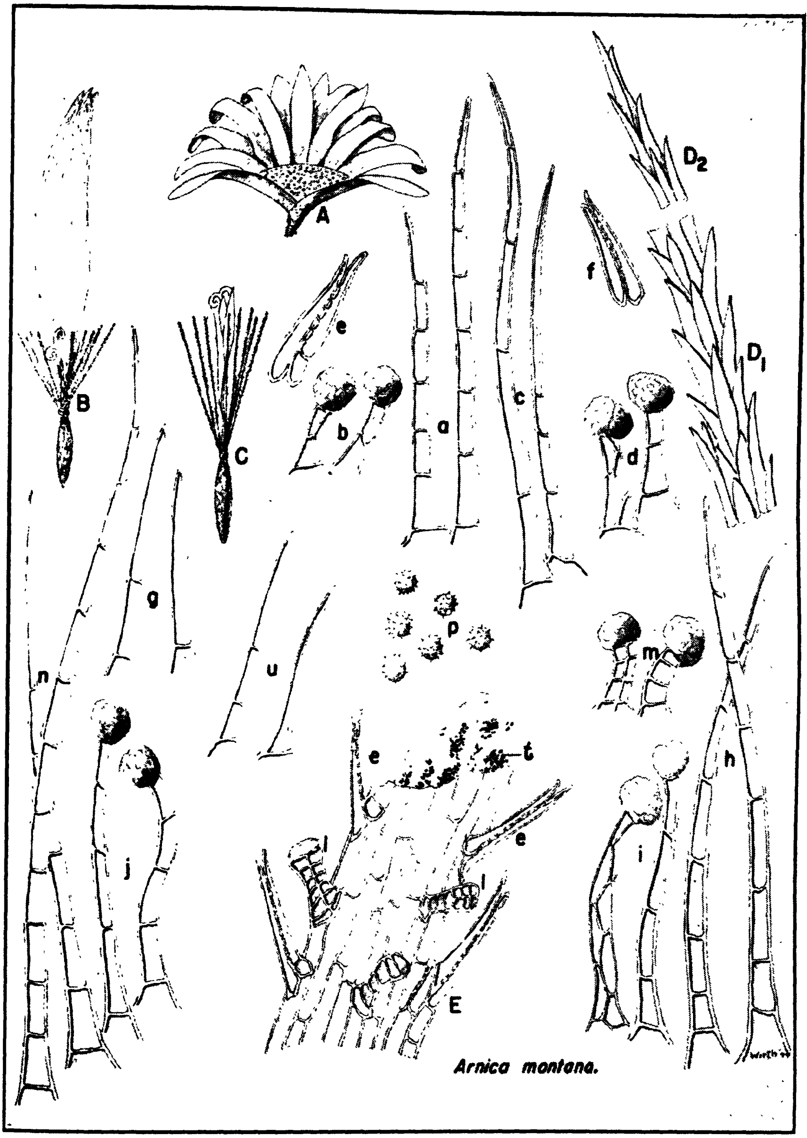


FIG. 349.—*Arnica montana.* *A*, receptacle with bracts; *B*, ligulate flower; *C*, tubular flower; D_1, pappus, lower portion; D_2, pappus, apical portion; *E*, surface fragment, ligulate achene; *a*, non-glandular hair, ligulate corolla; *b*, glandular hair, ligulate corolla; *c*, non-glandular hair, tubular corolla; *d*, glandular hair, tubular corolla; *e*, double hair, ligulate achene; *f*, double hair, tubular achene; *g*, non-glandular hair, receptacle; *h*, non-glandular hair, bract; *i*, glandular hair, bract; *j*, glandular hair, peduncle; *l*, glandular hair, ligulate achene; *m*, glandular hair, tubular achene; *n*, non-glandular hair, peduncle; *p*, pollen grains; *t*, phytomelane; *u*, non-glandular hair, tubular achene. (Receptacle × 1; ligulate and tubular florets × 2; all other elements × 65.) (Drawing by Wirth.)

STANDARDS.—Arnica contains not more than 3 per cent of foreign organic matter. The involucre and torus of the flower-heads are frequently injured on the plant or after collection, by larvæ of the insect *Trypeta arnicivora;* the German pharmacopœia requires their removal from the drug, the florets alone being used.

USES AND DOSE.—Arnica used orally, intravenously or locally is a stimulant, increasing temperature and secretions. When used internally, its effects are followed by transient depression and debility. Externally the tincture may be bactericidal, irritant and even vesicant, the flowers proportionately stronger than the root. It is used mostly as a vulnerary for bruises, sprains, abrasions, slight wounds, etc. Average dose, 0.1 gm.

MATRICARIA

Matricaria, Hungarian Chamomile or German Chamomile (U. S. P. 1842 to 1926; N. F. 1926 to date) is the dried flower-head of *Matricaria chamomilla* Linné. *Matricaria* is from the Latin *matrix,* in allusion to the medicinal effect on that organ; *chamomilla* is a contraction of *chamæmelum,* Greek for earth-apple, in allusion to the apple-like odor of its flowers. The plant is an annual herb, indigenous to Europe and western Asia and naturalized in Australia and parts of the United States. The mature flower-heads are collected from wild plants. Matricaria has a large domestic use, especially among Germans.

DESCRIPTION.—See Figure 350 and the National Formulary.

POWDER.—Color moderate yellowish brown to light olive brown; odor pleasantly aromatic; taste aromatic and bitter; pollen grains numerous, from 18 to 25 microns in diameter, nearly spheroidal or triangular from the 3 pores, the cuticle being very prickly; fragments of corolla with sessile, 8-celled glandular hairs; characteristic cells of anther; stigma with papillæ; cells of achenes having scalariform perforations in the walls; sclerenchymatous fibers of involucral scales.

CONSTITUENTS.—Volatile oil, about 0.25 per cent; anthemic acid in colorless, silky, very bitter needles, and with the odor of chamomile; anthemidin; malic acid; tannin. The volatile oil is viscid, dark blue (due to the presence of azulene), and strongly aromatic in odor and taste. When the oil is exposed to light and air, the color gradually fades to green, then brown, more rapidly so when the stem or involucre is present in the distilled drug.

STANDARDS.—Matricaria contains not more than 10 per cent of the stems of the plant and not more than 2 per cent of other foreign organic matter, and yields not more than 4 per cent of acid-insoluble ash.

USES AND DOSE.—Matricaria is a stimulant, a nervine, a carminative and a diaphoretic. Average dose, 15 gm.

ADULTERANTS.—In *Anthemis arvensis* the receptacle is solid and conical and the involucral scales are lanceolate. In *Anthemis cotula* the peduncles are slightly pubescent and the ligulate flowers neutral.

Spanish Chamomile, the flowering heads of wild grown *Anthemis nobilis,* contains more volatile oil and bitter principles than the cultivated drug and is probably more active, but more liable to produce nausea.

Anthemis, Roman or English Chamomile (U. S. P. 1820 to 1916), is the dried, expanded flower-head of *Anthemis nobilis,* a perennial herb indigenous to southern and western Europe and cultivated in Europe and the United States. The flowers are collected from cultivated plants, and dried by artificial means, the principal supplies coming from Belgium, France and Saxony.

The flower-heads are globular, compressed, 1.5 to 2 cm. in diameter; the involucre is hemispherical, with 2 or 3 rows of imbricated, nearly equal, somewhat elliptical, very pubescent scales, having a greenish middle portion and a yellowish margin; the receptacle is conical or convex, solid, 3 to 4 mm. in height, occasionally hollow, and sometimes containing the larvæ of an insect and with chaff-scales resembling the involucral scales, about 2 mm. in length; the ligulate florets are numerous, 6 to 10 mm. in length, with a white, 3-toothed, 4-nerved corolla; a glandular ovary about 1 mm. in length, a slender style and bi-cleft stigma; the tubular florets are few or none, lemon-yellow, perfect; the achene oblong; without pappus; the odor distinct and the taste aromatic and bitter.

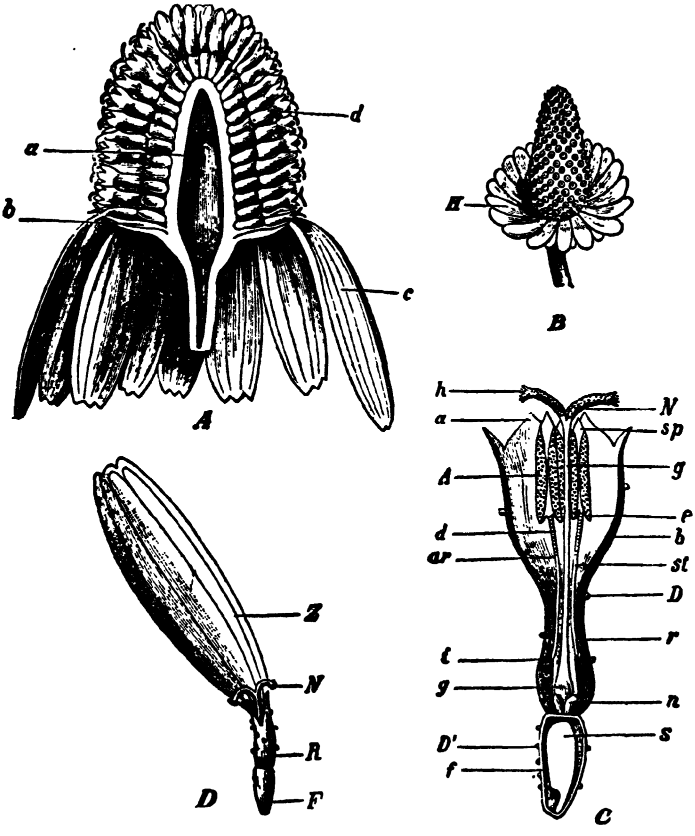


FIG. 350.—Matricaria: *A*, longitudinal section of the conical head 3 to 10 mm. in breadth: *a*, the narrow, conical, hollow receptacle and short peduncle; *b*, involucre of 20 to 30 imbricate, oblanceolate, pubescent scales, brownish with whitish margins; *c*, 10 to 20 pistillate ray florets, about 12 mm. in length and with a white 3-toothed, 4-veined corolla; *d*, numerous, yellowish, perfect disk florets about 2.5 mm. in length; achenes somewhat obovoid, about 0.5 mm. in length, faintly 3- to 5-ribbed, without pappus. *B*, Head with the florets removed, showing the long conical receptacle and the involucre (*H*). *C*, Tubular floret showing the ovary (*f*) with glandular hairs (*D'*) and the embryo (*S*), which develops after fertilization; style (*g*) and bifid stigma (*N*), the surface of which is covered with hairs; *n*, nectaries; *b*, corolla tube with narrow lobes (*a*); stamens showing filament (*st*), united anthers (*A*) and apex of connective (*sp*). *D*, Ligulate floret showing ovary (*F*) and bifid stigma (*N*); tube of corolla (*R*) and the upper ligulate portion (*Z*). (After Meyer.)

Microscopic mounts show bract fragments having scattered, somewhat thick-walled unicellular hairs and occasional sessile glandular hairs; pollen grains, occasional, spheroidal, about 30 microns in diameter, the cuticle being very prickly; sclerenchymatous fibers about 10 microns in width and having very thick walls; papillæ of corolla and stigma; small rosettes of calcium oxalate occasionally present; characteristic cells of anther.

Anthemis contains a volatile oil, which is bluish green when fresh, 0.8 to 1 per cent; a bitter crystalline glucoside, anthemisol; anthemic acid (see matricaria); 5.25 per cent of resin; 1.5 per cent of a bitter crystalline wax; and tannin. The volatile oil consists principally of the isobutyl, amyl and hexyl esters of butyric, angelic and tiglic acids, anthemol, an isomer of camphor, and azulene, hence dark blue in color.

Anthemis is a stimulant, a carminative, a nervine and a tonic. In large doses it is an emetic.

Calendula, or Marigold (U. S. P. 1882 to 1916; N. F. 1916 to 1947) is the dried ligulate floret of *Calendula officinalis* Linné. The plant is an annual herb indigenous to southern Europe and the Levant, and widely cultivated as a garden plant. The flowers are collected when fully expanded and then dried.

Some of the drug is produced in the United States, but most of it is imported from Spain, France and Italy. Marigold has been known from the beginning of documentary records. It was introduced into America by the early colonists.

The florets are usually without the ovary; corolla bright yellow, 15 to 25 mm. in length, 1- to 3-toothed, 4- to 5-veined, margin nearly entire, tube sometimes enclosing the remains of a filiform style and bifid stigma, pubescent on the outer surface; ovary oblong, about 0.5 mm. in length, pubescent. The powder is bright yellow; odor distinct; taste faintly saline, slightly bitter; epidermal cells narrow, elongated, having sinuous walls, numerous oily globules and irregular chromoplastids; pollen grains spheroidal, about 40 microns in diameter, having 3 pores and a spinose cuticle; non-glandular hairs consisting of a double row of cells having a 1- or 2-celled apex and up to 950 microns long; calcium oxalate in rosettes from 2 to 6 microns in diameter. On adding the powder to water the latter becomes a pale straw-color.

Calendula contains volatile oil; an amorphous bitter principle; a gummy substance, calendulin, which forms with water a transparent mucilage that is not precipitated by tannin; resin. Natural ash, 9.3 per cent, with 1.7 per cent of acid-insoluble ash.

Calendula is a stimulant and a carminative. Average dose, 1 gm.

ADULTERANTS.—The florets of various *Compositæ* are sometimes admixed with or substituted for calendula. Of these the following may be mentioned together with their principal distinguishing characteristics. The ligulate corolla of *Taraxacum officinale* is 5-toothed; the ligulate corolla of *Arnica montana* is 7- to 12-veined; the ligulate corolla of *Tussilago farfara* is linear, about 13 mm. in length and about 0.3 mm. in breadth, summit acute, entire; and the ray florets of *Tagetes patula* are somewhat spatulate, about 20 mm. in length and 10 mm. in width, sometimes marked with darker stripes, and have undulate margins.

Cotula, Mayweed or Wild Chamomile (U. S. P. 1820 to 1882) is the dried herb of *Anthemis Cotula* Linné, a plant indigenous to Europe, but now naturalized as a common weed in many parts of North America. The stem grows to be 30 mm. high with ascending branches from the base upward; leaves sessile, obovate, thrice ternately divided into linear lobes. The flower-heads terminate the branches; the receptacle is conical, solid; the ray florets white, 3-toothed; the disk florets yellow, with ribbed akenes and without pappus. The odor is fetid aromatic; the taste bitter and acrid.

CONSTITUENTS.—A little volatile oil, resin, tannin, valeric and oxalic acids, an acrid fatty substance. The drug is more acrid than the English Chamomile; the juice of the fresh leaves will blister the skin. It has been used as a sudorific and antispasmodic, in colic and dysmenorrhea.

SANTONICA

Santonica or Levant Wormseed (U. S. P. 1863 to 1916) is the dried flower-heads of *Artemisia Cina* Berg.

Santonin (U. S. P. 1863 to 1942; N. F. 1942 to date) is the inner anhydride of santoninic acid ($C_{15}H_{18}O_3$) and obtained from santonica.

Artemisia was named for Queen Artemisia, wife of King Mausolus, who first employed it. The plant is a small shrub indigenous to the deserts of Russian Turkestan, from whence most of the commercial supply has come. It is now cultivated in western Washington state, and during World War II, the production of drug there has greatly increased. The flower-heads are collected in July and August before they expand, and are carefully dried and preserved. If the flower-heads are unexpanded and quickly dried they will yield over 3 per cent of santonin; just so soon as the flower matures, however, there is a rapid disappearance of the anthelmintic principle.

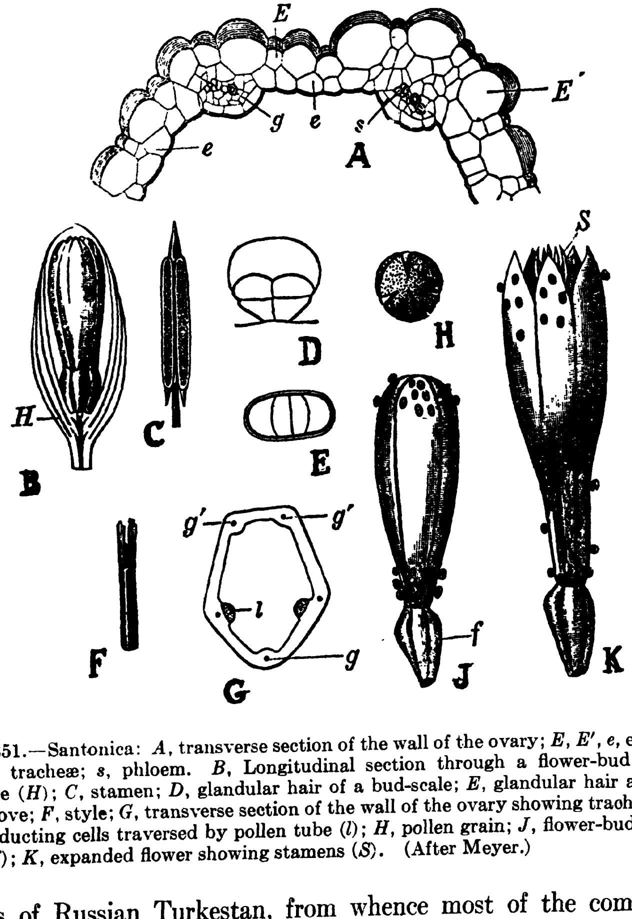


FIG. 351.—Santonica: *A*, transverse section of the wall of the ovary; *E*, *E'*, *e*, epidermal cells; *g*, tracheæ; *s*, phloem. *B*, Longitudinal section through a flower-bud showing involucre (*H*); *C*, stamen; *D*, glandular hair of a bud-scale; *E*, glandular hair as viewed from above; *F*, style; *G*, transverse section of the wall of the ovary showing traoheæ (*g*, *g'*) and oonducting cells traversed by pollen tube (*l*); *H*, pollen grain; *J*, flower-bud showing ovary (*f*); *K*, expanded flower showing stamens (*S*). (After Meyer.)

Santonica.—The flower-heads are oblong or ellipsoidal, 2 to 4 mm. in length, 1 to 1.5 mm. in diameter; the involucre is ovoid, consisting of 12 to 18 closely imbricated, ovate or ovate-lanceolate, glandular, somewhat shiny bracts, about 2 mm. in length, with a yellowish green or greenish brown middle portion and whitish margin; the receptacle is flat, naked, with 3 to 6 unexpanded, perfect, tubular flowers about 1.5 mm. in length and completely enclosed by the upper bracts; the ovary is oblong and without pappus; the odor is distinct and the taste aromatic.

See Figure 351 for the structure.

The powder is light grayish brown, with nearly smooth spheroidal pollen grains from 15 to 20 microns in diameter, and having 3 pores; glandular hairs are of two kinds, either with 1 or 2 short cells or with 2 to 3 pairs of cells.

The drug contains santonin, 2 to 3.5 per cent; volatile oil about 2 per cent, consisting chiefly of cineol, some terpineol, terpinene and inactive pinene; a crystalline principle, artemisin, which is apparently oxysantonin; and a resin.

Santonin crystallizes in rhombic prisms, becoming yellow on exposure to light; it is nearly insoluble in water and sparingly soluble in alcohol; and is colored red by alcoholic solutions of the alkalis.

Santonica and santonin are anthelmintics. Average dose of santonin, 60 mg.

ALLIED PRODUCTS.—*Artemisia gallica*, or French Wormwood contains santonin and about 1 per cent of a volatile oil.

A santonin-free santonica has been found in the markets of Europe and of this country.

The seed of *Quisqualis indica* (Fam. *Combretaceæ*) or Rangoon Creeper furnishes a substitute for santonica. The plant grows wild in the tropical regions of Asia, America and Africa. The best drug comes from the province of Szechwan, which furnishes it in large quantities. The seed contains an active principle resembling santonin and possesses anthelmintic properties. The maximum dose is 7.5 gm. for adults.

GRINDELIA

Grindelia or Grindelia Robusta (U. S. P. 1882 to 1926; N. F. 1926 to date) consists of the dried leaves and flowering tops of *Grindelia camporum* Greene, of *Grindelia humilis* Hooker and Arnott, or of *Grindelia squarrosa* (Pursh) Dunal. Grindelia was named for D. H. Grindel, a Russian botanist, who died in 1836; *squarrosa* means scabby or scurfy, in reference to the appearance of the plant; *camporum* means a bell and refers to the shape of the flowers. The plants are perennial herbs of western North America. *Grindelia squarrosa* grows on the borders of California and Mexico extending northward to Canada; *Grindelia camporum,* the common gum plant of California, is found extensively in the western and central desert portions of California. Grindelia is collected in early summer, when the leaves and flowering tops are covered with a resinous exudation, and dried.

Grindelia was used by the California Indians and was known to the early Jesuit missionaries. In 1863 Canfield used it as a remedy for ivy poisoning, and in 1875 it was introduced into medicine.

DESCRIPTION AND STRUCTURE.—See Figures 352 and 353 and the National Formulary.

POWDER.—Light yellowish brown to yellow; odor balsamic; taste aromatic, bitter and resinous; in the leaf epidermis are groups of broadly elliptical stomata, about 35 microns in length, having wide pores, which project above the leaf surface; and the depressed, glandular hairs, having an irregular, ellipsoidal, multicellular head up to 100 microns in diameter, each cell of which contains a rosette from 5 to 8 microns in diameter. Cells of mesophyll spheroidal, filled with large chloroplasts, about 10 microns in diameter; large, somewhat elongated, thick-walled, colorless cells of water-storage tissue; pollen grains spheroidal, about 35 microns in diameter, having 3 pores and a spinose cuticle; stem fragments showing tracheæ having annual and spiral thickening and simple or bordered pores, associated with numerous narrow, strongly lignified wood fibers; pith cells more or less tabular and containing a layer of protoplasm in which are embedded numerous spheroidal granules.

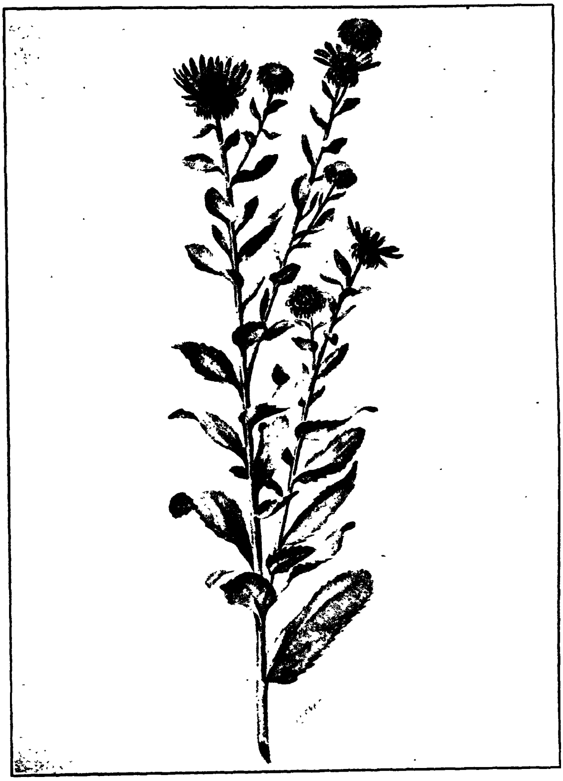


Fig. 352.—Scaly Grindelia (*Grindelia squarrosa*). Flowering plant showing the oblong, sharply serrate, sessile leaves; and the heads, composed of numerous imbricated, squarrosely tipped or spreading scales, the yellow, ligulate ray florets directed upwards, and the central cone of numerous tubular florets. (From Bulletin 219, Bureau of Plant Industry, U. S. Department of Agriculture.)

Constituents.—Resins about 21 per cent; a phytosterol glucoside, grindelol; a bitter crystalline alkaloid, grindeline; a levorotatory sugar; tannin 1.5 per cent; a volatile oil having the characteristic odor of the drug; about 8 per cent of ash.

Standards.—Grindelia contains not more than 10 per cent of its stems over 2 mm. in diameter.

Uses and Dose.—Grindelia is used as a sedative, an antispasmodic and an expectorant. The fluidextract is used in the treatment of poisoning by *Rhus toxicodendron*. Average dose, 2 gm.

ALLIED PLANTS.—Other species of *Grindelia* growing in the western United States and Mexico are similarly employed, as *G. hirsutula*, the stems of which are purplish red and pubescent; and *G. glutinosa*, in which the leaves are glabrous and rounded at the apex, the pappus being 5- to 8-toothed.

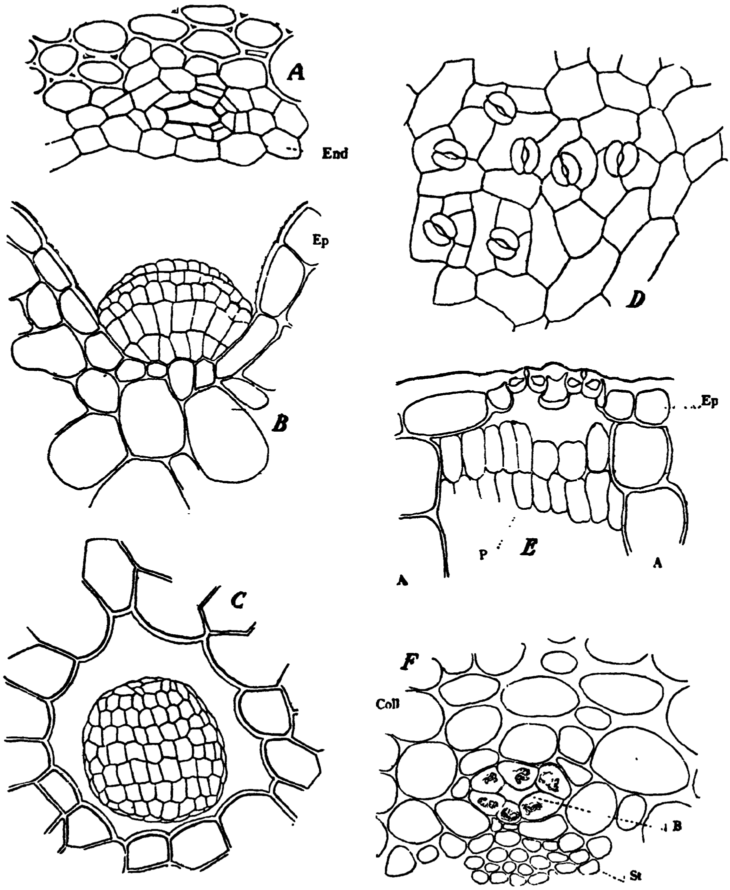


FIG. 353.—*Grindelia squarrosa: A*, transverse section of a portion of the stem, showing a large resin canal bordering on the endodermis (*End*). *B*, Transverse section of a portion of a leaf showing the epidermal cells (*Ep*), and a large sessile glandular hair, in the depressed epidermal layer. *C*, Surface view of a glandular hair, situated in a wide cavity of the epidermis. *D*, Surface view of the epidermal cells from the dorsal surface of the leaf, showing a small group of stomata. *E*, Transverse section of the dorsal layers of the leaf showing the epidermal cells (*Ep*), having thick outer walls and 2 of the stomata; palisade cells (*P*); and part of the water-storage tissue (*A*). *F*, Transverse section of part of a midrib of the leaf; *Coll*, collenchyma; *B*, a resin canal; *St*, the fibrous pericycle. (After Holm.)

EUPATORIUM

Eupatorium, Thoroughwort or Boneset (U. S. P. 1820 to 1916; N. F. 1926 to date) consists of the dried leaves and flowering tops of *Eupatorium perfoliatum* Linné. *Eupatorium* was named in honor of Eupator, King of Pontus, who is said to have used one of the species in medicine; *perfoliatum* means having a sessile, clasping leaf.

The plant is a perennial herb (Fig. 354) indigenous to eastern and central North America. The drug was used as a domestic remedy by the early colonists. It was a favorite remedy in the practice of American medicine at least a hundred years before there was a print in an American materia medica.

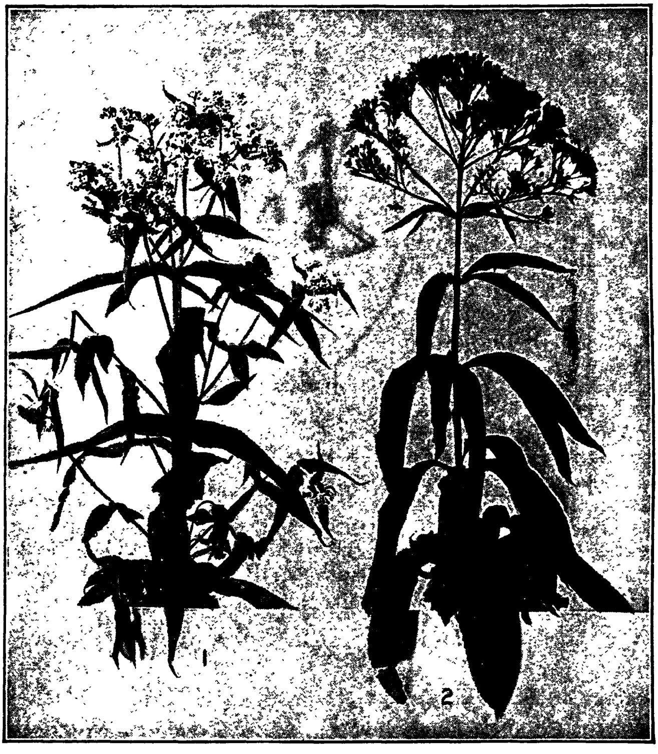


Fig. 354.—1. *Eupatorium perfoliatum* with opposite, connate-perfoliate leaves and cymose-paniculate inflorescence. 2. *Eupatorium purpureum* with verticillate, petiolate leaves, and a large terminal panicle of flowers.

Description.—Usually in more or less broken fragments. Leaves lanceolate opposite, 10 to 20 cm. in length, 2 to 5 cm. in breadth; apex acuminate; base connate-perfoliate; margin crenate-serrate; upper surface light olive to dark yellowish green, rugose and mostly glabrous; under surface paler, tomentose, and dotted with minute, glistening, yellow resin masses. Flower-heads are small, numerous and corymbed, receptacle flat; involucre light green, oblong; the scales imbricate, linear-lanceolate, hairy; corolla 5-toothed, whitish; anthers purplish, included; style deeply cleft, much exserted. Achenes 5-angled, pappus consisting of a single row of about 20 rough bristles.

Powder.—Weak yellow to light olive; odor faintly aromatic; taste strongly bitter; non-glandular hairs 2- to 8-celled, finely striate, thin-walled, the end cells pointed or somewhat rounded; glandular hairs short-stalked and with multicellular heads up to 80 microns in diameter; pollen grains ellipsoidal, up to 25 microns in diameter, and with numerous, spiny, centrifugal projections; pappus occurring as a multicellular axis about 30 microns in diameter and with short, unicellular alternate branches; tracheæ spiral, annular, or with bordered pores; sclerenchymatous fibers thin-walled, non-lignified, having few, simple, oblique pores, numerous fragments of leaf epidermis showing elliptical stomata 18 to 36 microns in length; achene pericarp with cells having characteristically thickened, brown to yellow walls; occasional fragments of stem tissues; and of corolla tissues.

CONSTITUENTS.—Volatile oil; a bitter, crystalline glucoside, eupatorin; resin; a crystalline wax; a glucosidal coloring principle related to tannin but crystallizing in small yellow needles and giving an orange-red precipitate with lead acetate solution; a glucosidal tannin, which is colored deep green with ferric chloride and gives a yellow precipitate with lead acetate solution; gallic acid; total ash, 7.5 to 9.9 per cent.

STANDARDS.—Eupatorium contains not more than 10 per cent of its stems.

USES AND DOSE.—Eupatorium is used as a stimulant and diaphoretic; in large doses it is also an emetic and a cathartic. Average dose, 2 gm.

Eupatorium Teucrifolium or Wild Horehound (U. S. P. 1820 to 1842) consists of the leaves and flowering tops of *Eupatorium teucrifolium* Willdenow. The leaves are alternate, lanceolate to oblong-ovate, rather truncate, and serrate toward the base. The plant is found from Massachusetts to Louisiana. The drug resembles that from *Eupatorium perfoliatum.*

Eupatorium Purpureum, Joe-pye Weed or Gravel-root (U. S. P. 1820 to 1842) consists of the rhizome and roots of *Eupatorium purpureum* Linné. The plant is common (see Fig. 354) in low grounds in eastern and central North America, and is a tall stout herb, with oblong-lanceolate leaves, 3 to 6 in a whorl, and light purplish red flowers in dense corymbs. Purple boneset contains a volatile oil, 0.07 per cent; a yellow crystalline principle, euparin, which somewhat resembles quercitrin; resin, 0.25 per cent; calcium oxalate, 1.82 per cent; and ash, 14 per cent.

Dog-fennel (*Eupatorium capillifolium* [Lam.] Small, or *E. fœniculaceum* Willd.), a perennial herb, with alternate, 1- to 2-pinnately parted leaves and white flowers, which is common in the Southern States, and yields a volatile oil which contains considerable phellandrene. The juice of the herb is used for relieving pain from the bites of insects.

TARAXACUM

Taraxacum or Dandelion Root (U. S. P. 1831 to 1926; N. F. 1926 to date) consists of the dried rhizome and roots of *Taraxacum officinale* Weber or *Taraxacum lævigatum* DeCandolle. *Taraxacum* probably is from the Greek *taraxis* meaning inflammation of the eye, for which the juice is used; *lævigatum* is Latin meaning smooth or to make smooth. The drug is mentioned in the writings of Hippocrates, Galen, Paulus and Avicenna (980–1037), and other physicians down to the present day. The plant is a perennial herb indigenous to Europe and Asia, but now naturalized in all civilized parts of the world.

The drug should be collected either directly before or after the vegetative activity of the plant. It is used in either the fresh or dry condition, and should be protected against the development of insects.

DESCRIPTION.—Somewhat cylindrical, tapering, flattened and branched, 6 to 15 cm. in length, and often broken into irregular pieces; externally moderate yellowish brown to brownish black, wrinkled with numerous rootlet scars; crown simple or branched, slightly annulate from numerous leaf bases; fracture short, horny when dry, tough when damp; internally bark light brown, 2 to 6 mm. in thickness, made up of concentric layers of laticiferous vessels and sieve alternating with white parenchyma; wood lemon-yellow, 1 to 4 mm. in thickness, porous and non-radiate; odor slight; taste bitter.

STRUCTURE.—See Figure 355 and the National Formulary.

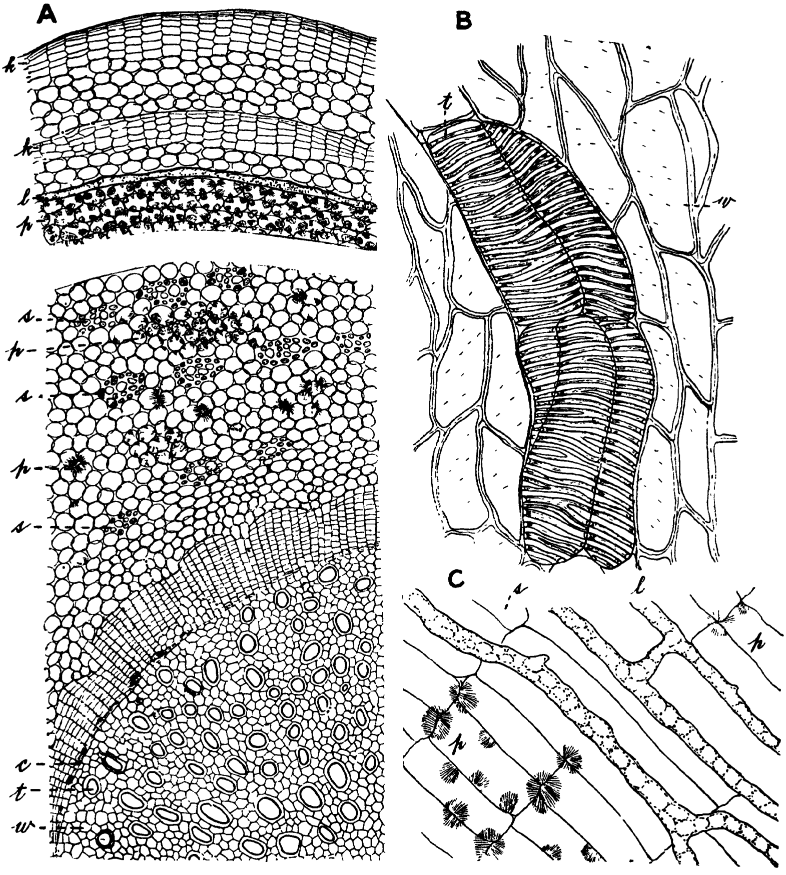


FIG. 355.—Taraxacum: *A*, transverse section of root showing cork (*k*), parenchyma containing inulin (*p*), laticiferous vessels (*l*), phloem groups (*s*) composed of sieve and laticiferous vessels, cambium (*c*), tracheæ (*t*), modified, non-lignified wood fibers (Ersatzfasern) (*w*). *B*, Longitudinal section of xylem showing several of the reticulate tracheæ and the modified wood fibers with oblique pores that are apparent in preparations made with zinc chloriodide. *C*, Longitudinal section of a phloem group showing branching laticiferous vessels (*l*), sieve cells (*s*), and parenchyma (*p*) containing sphero-crystals of inulin.

POWDER.—Pale brown to weak yellowish orange; odorless; taste bitter; parenchyma cells large, thin-walled and with irregular, glistening masses of inulin; fragments with brown to yellow, anastomosing laticiferous vessels; spiral and reticulate tracheæ and non-lignified wood fibers, with simple, irregular or oblique pores; starch is absent.

CONSTITUENTS.—A bitter, amorphous, dark-colored substance; inulin about 25 per cent; a volatile oil; an enzyme; levulose; choline; para-hydroxyphenylacetic acid; 3:4-dihydroxycinnamic acid; a mixture of fatty acids; two monohydric alcohols, taraxasterol and homotaraxasterol; and a substance which has been designated "cluytianol" (see *Cluytia similis*), but which apparently is a phytosterol glucoside.

STANDARDS.—Taraxacum contains not more than 2 per cent of foreign organic matter, and yields not more than 4 per cent of acid-insoluble ash.

USES AND DOSE.—Taraxacum is a diuretic, a tonic and an aperient. Average dose, 4 gm.

Chicory, Succory, or Blue Dandelion Root is the rhizome and roots of *Cichorium intybus*, a perennial herb, indigenous to Europe and localized throughout the northern United States and Canada. The rhizome, with its continuation the root, is upright, fusiform and deep-seated. The drug should be collected in the early spring or the fall, from younger plants, sliced to aid rapid drying, and preserved against moisture and insect attacks.

Chicory somewhat resembles taraxacum, but the outer surface is light or dark brown, and irregularly, often spirally wrinkled; the inner surface shows a thick bark, having radiating strands of phloem; a yellowish wood having narrow radiating medullary rays and xylem wedges with broad tracheæ.

The powder shows free masses of inulin, which, in roasted chicory, are dark brown, soft, sweetish, sinking in water, but dissolving to form a brownish solution; irregular masses of inulin in the parenchyma cells; branching latex vessels up to 10 microns in width; tracheæ short, more or less cylindrical, with pointed ends, from 100 to 200 microns in length, and having large, elliptical, simple pores.

Chicory is sometimes adulterated with the roots of dandelion, carrot, beet and turnip, as well as cereal products. It is a tonic and a diuretic. When roasted, it is used as a substitute for or an adulterant of coffee.

Inula or Elecampane (U. S. P. 1820 to 1916; N. F. 1916 to 1936) is the dried rhizome and roots of *Inula Helenium* Linné, a large perennial herb, indigenous to central Europe and Asia and naturalized from Canada to North Carolina. The drug should be collected in the early spring or the fall from younger plants, sliced to aid rapid drying and preserved against moisture and insect attacks.

When entire it is fusiform, irregularly branching, the crown being somewhat annulate and surmounted by a stem-scar, the lower portion being longitudinally wrinkled; usually in irregular pieces; externally light to dark brown, longitudinally wrinkled, with short roots or circular root-scars and occasionally having the cork more or less abraded, showing a grayish white cortex; fracture tough, horny and somewhat uneven; internally light brown, showing a distinct cambium and numerous large resin canals in both the xylem and cortex; odor distinct, aromatic; taste sweetish, aromatic, slightly acrid and pungent.

Older rhizomes where a broad continuous ring of wood occurs should be rejected. The roots show a structure similar to that of younger rhizomes, but without a pith; the primary tracheæ are associated with elongated, thin-walled cells with reticulate perforations.

The powder is very light brown; on boiling with water it emits a distinct aromatic, pepper-like odor, distinguishing it from belladonna; it shows inulin in the parenchyma cells, mostly in the form of separate, irregular, colorless granules, up to 30 microns in diameter; fragments of yellowish brown or reddish brown resin masses from the large resin canals in cortex and medullary rays; tracheæ having narrow lumina and large elliptical perforations or occasionally bordered pores; very narrow, strongly lignified wood fibers marked by numerous simple pores; fragments of cork with rectangular or somewhat polygonal cells having relatively thin brownish walls, the cells usually containing a granular cytoplasm and nucleus; small groups of narrow, elongated sclerenchymatous fibers; fragments of resin canals with thin-walled epithelial cells.

Inula contains inulin, 35 to 45 per cent; alantol, 1 to 2 per cent, consisting chiefly of helenin, with small quantities of alantolic acid, camphor and isohelenin; a bitter principle; inulenin, pseudoinulin and mucilage. Total ash 4.4 per cent; acid-insoluble ash 0.3 per cent. **Alantol** is obtained by distillation with water or steam, and is an oily substance with the odor and taste of peppermint. **Helenin,** alantolactone or elecampane camphor is a stearoptene in white crystals, volatile in steam, almost insoluble in water, but readily soluble in most of the volatile solvents. Both of these products have been used as antiseptics and expectorants in throat and bronchial infections. Dose of helenin, 10 to 20 mg.; maximum dose daily 100 mg. **Phytomelane** (see Fig. 357), a brown or nearly black, carbon-like substance occurs occasionally in the intercellular spaces between the parenchyma cells.

Through carelessness, belladonna root is sometimes substituted for inula. The former is characterized by containing starch and having a distinct heavy odor (see Belladonnæ Radix).

Inula is an aromatic stimulant; it is used also as an expectorant, a diaphoretic and a diuretic.

Inulin or Hydrous Inulin (N. F. 1936 to date, as reagent) is a fructosan $(C_6H_{10}O_5)_n{:}XH_2O$, obtained from the subterranean organs of members of the family *Compositæ.* It is especially abundant in Taraxacum, Inula, Lappa and Pyrethrum rhizome and roots. Inula occurs in the cell sap; by immersing the fresh rhizome or root in alcohol for some time the inulin usually crystallizes in sphærite aggregates. Upon drying the plant part it forms refractive masses, more or less filling the parenchyma cells. It is readily soluble in hot water, slightly so in cold water or in alcohol. Its aqueous solution is levorotatory and neutral to litmus paper. Inulin is used in culture media as a fermentative identifying agent for certain bacteria, and in laboratory methods for the evaluation of renal function.

Lappa or Burdock Root (U. S. P. 1831 to 1842, 1851 to 1916; N. F. 1916 to 1947) is the dried first-year root of *Arctium Lappa* Linné or of *Arctium minus* Bernhardi. *Arctium,* Greek, means a bear and a plant, in reference to the persistent burrs; *Lappa* is Latin for burr; and *minus,* Latin, refers to the smaller species.

The plants are biennial herbs indigenous to Europe and northern Asia and naturalized in waste places in the United States and Canada. The fleshy root is collected in autumn from plants of the first year's growth and carefully dried. Most of the commercial supplies come from Belgium, France and Germany. Burdock has been used in domestic medicine from time immemorial.

The drug is nearly cylindrical, slightly tapering, or broken and split longitudinally into pieces, 5 to 20 mm. in diameter; externally moderate brown to weak yellowish orange, longitudinally wrinkled, with few rootlets or rootlet scars, crown somewhat annulate from scars of bud-scales and sometimes surmounted by a soft, woolly tuft of leaf remains having unicellular, twisted hairs; fracture short, horny when dry, tough when damp; internally weak brown to weak yellow, radiate, bark 2 to 3 mm. in thickness, wood porous, cambium zone distinct. Odor slight; taste mucilaginous, slightly bitter.

Old woody roots in which the center is more or less obliterated and which have been collected from the fruiting plant should be rejected.

The periderm consists of thin-walled, brownish, rectangular cork cells; cortex of inulin-bearing parenchyma, the inner layer having narrow strands of phloem; cambium distinct; xylem composed of narrow wedges, made up mostly of parenchyma, and a few thin-walled wood fibers and wide tracheæ, separated by broad medullary rays; the wood parenchyma and medullary rays contain inulin in the form of highly refractive, irregular masses, varying from 6 to 45 microns in length; tracheæ from 50 to 150 microns in width, and marked by numerous narrow, simple pores and occasionally accompanied by narrow thin-walled wood fibers. Tissues of the pericycle and primary cortex are commonly seen in the outer layers of the bark. The outer cortical region shows an interrupted circle of resin canals, which are wanting in older roots.

Lappa contains inulin, about 45 per cent; about 0.07 per cent of a volatile oil; a bitter principle; about 0.04 per cent of a fixed oil; resin; tannic acid; mucilage; and a sugar. Total ash, 4 per cent; acid-insoluble ash, 0.15 per cent.

Lappa contains not more than 4 per cent of attached leaf bases, and yields not more than 3 per cent of acid-insoluble ash, not less than 8 per cent of alcohol-soluble extract, and not more than 10 per cent of crude fiber. A good quality of drug yields from 12 to 18 per cent of alcohol-soluble extractive.

Lappa is a diuretic, a diaphoretic and an alterative. Average dose, 2 gm.

Arctium Lappæ Semina, Fructus Lappæ or Burdock Fruit (Seed) (U. S. P. 1831 to 1842) is the ripe fruit of *Arctium Lappa* Linné.

The fruits (seed) are about 6 mm. long; obovate-oblong, wrinkled, mostly deprived of pappus hairs; gray-brown, mottled with black; inodorous; oily and bitter in taste. The fruits contain lappine, a bitter crystalline alkaloid; resin about 1 per cent; a light yellow fixed oil, about 15 per cent. Average dose of the 10 per cent tincture, 10 cc.

ECHINACEA

Echinacea or Cone Flower (N. F. 1916 to date) consists of the dried rhizome and roots of *Echinacea pallida* (Nuttall) Britton or of *Echinacea angustifolia* (DeCandolle) Heller. *Echinacea* is from the Greek *echinos* meaning hedgehog, in reference to the rough-bristly leaves and stems of some species; *angustifolia*, Latin, means narrow-leaf, *pallida*, Latin, means pale. The plants are perennial herbs, *E. angustifolia* being the purple cone-flower of the southwestern United States, and *E. pallida* occurring throughout the central United States and extensively cultivated as cone-flower. The rhizomes and roots are collected from well-developed plants in the autumn and carefully dried (Fig. 357). Most of the commercial supply comes from Kansas.

DESCRIPTION.—Nearly entire, cylindrical, very slightly tapering; 10 to 20 cm. in length, 4 to 15 mm. in diameter; externally pale brown to moderate yellowish brown; lightly annulate in the upper portion, with occasional V-shaped stem-scars, somewhat wrinkled longitudinally, or furrowed and occasionally spirally twisted; fracture short, fibrous; internally, bark less than 1 mm. in thickness, wood thick and composed of alternate light- and dark-colored wedges; a circular pith in the rhizome; odor faint, aromatic; taste sweetish, followed by an acrid and tingling sensation resembling that of aconite, but lacking the persistency and numbing qualities of the latter.

STRUCTURE.—See Figure 356 and the National Formulary.

CONSTITUENTS.—Inulin, 5.9 per cent; inuloid, 6 per cent; sucrose, 7 per cent; vulose, 4 per cent; betaine, 0.1 per cent; resins, 1.9 per cent, consisting of two isomeric phytosterols; phytosterolin; and the following fatty acids: oleic, linolic, cerotic and palmitic. Echinacea probably also contains a glucoside. Total ash, 4.75 per cent; acid-insoluble ash, 0.45 per cent.

STANDARDS.—Echinacea contains not more than 3 per cent of foreign organic matter, and yields not more than 2 per cent of acid-insoluble ash. Echinacea which has lost its characteristic odor and taste must not be used.

USES AND DOSE.—Echinacea is a diaphoretic and an alterative. Average dose, 1 gm.

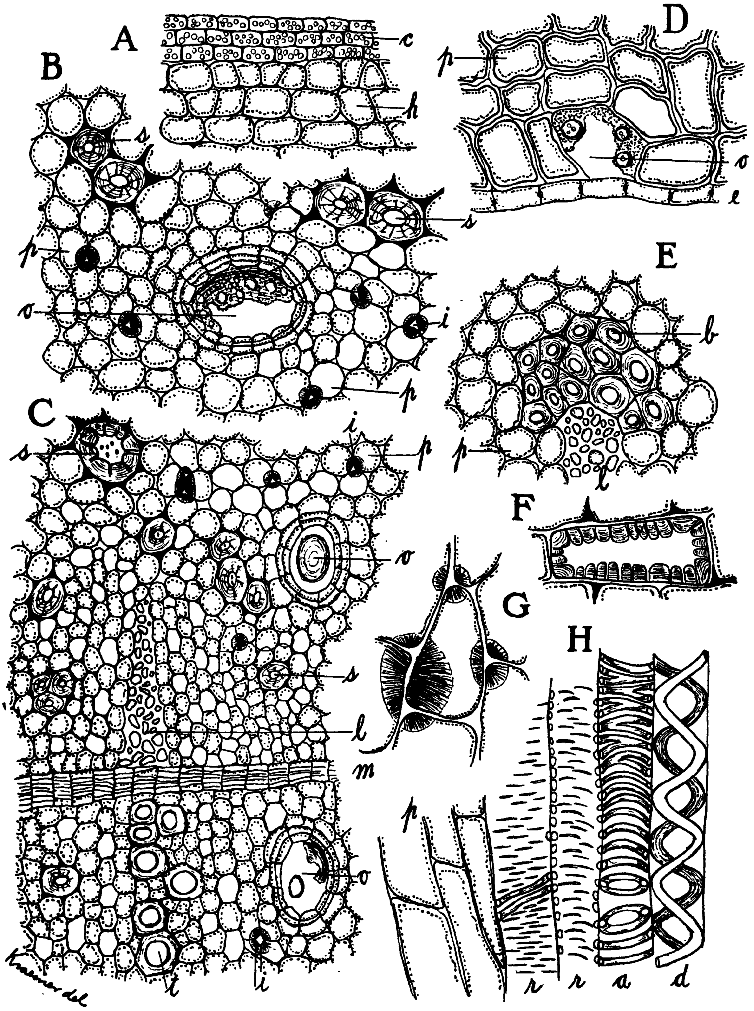


FIG. 356.—Echinacea: *A*, cross-section of outer layers of root, showing cork (*c*) and hypodermis (*h*); *B*, cross-section of cortex showing parenchyma (*p*), spherocrystals of inulin (*i*), sclerotic cells (*s*) associated with phytomelane, a carbon-like material found in the intercellular spaces adjacent to the stone cells; and oleoresin reservoirs or canals (*o*); *C*, cross-section of portion of fibrovascular bundle showing sieve (*l*), cambium (*m*), tracheæ (*t*), oleoresin canals (*o*), stone cells (*s*), parenchyma (*p*) and inulin crystals (*i*); *D*, cross-section near endodermis, showing endodermal cells with suberized radial walls and Casparyan spots (*e*), endodermal resin canal (*o*), and parenchyma (*p*); *E*, cross-section of rhizome showing a group of bast fibers (*b*), phloem (*l*), and parenchyma (*p*); *F*, a sclerotic cell; *G*, parenchyma with spherocrystals of inulin adhering to the walls; *H*, longitudinal section showing various forms of tracheæ: *d*, double spiral; *a*, annular; *r*, with simple pores; *p*, adjoining parenchyma.

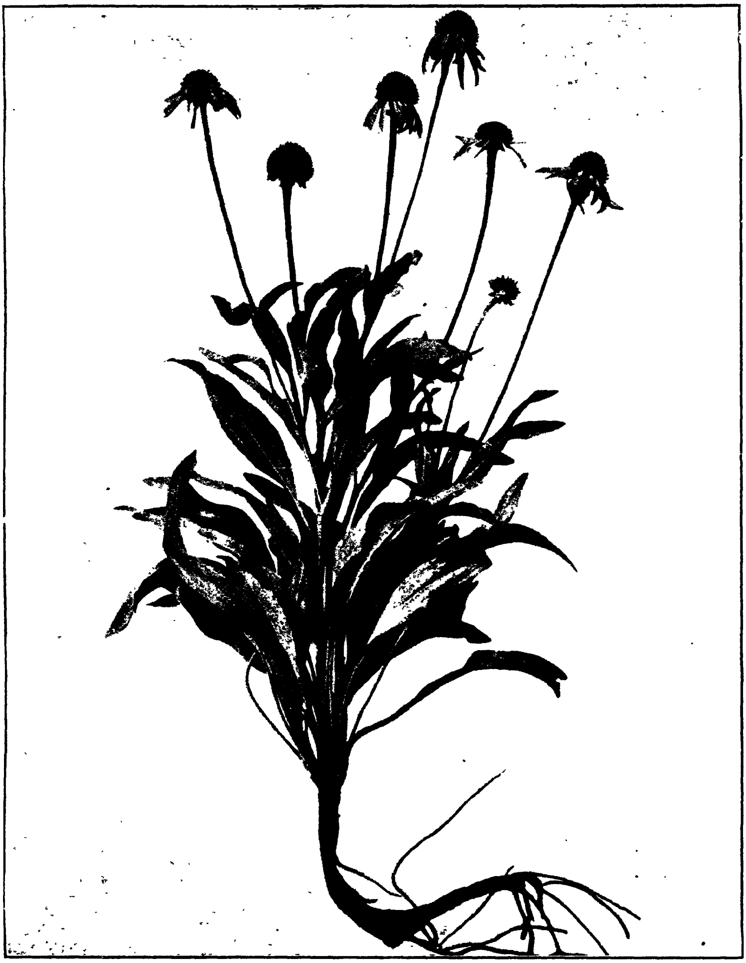


FIG. 357.—An entire plant of *Echinacea angustifolia* showing the lanceolate 3-nerved leaves and the conial heads with reflexed, ligulate ray florets. (From Year Book, U. S. Department of Agriculture.)

PYRETHRUM

Pyrethrum, Pyrethri Flores or Insect Flowers (N. F. 1947 to date) is the dried flower-head of *Chrysanthemum cinerariæfolium* (Treviranus) Bocc., *Chrysanthemum coccineum* Willdenow (*C. roseum* Weber and Mohr) or of *Chrysanthemum Marschalli* Aschers. Pyrethrum yields not less than 0.5 per cent of total pyrethrins (Pyrethrin I and Pyrethrin II).

Chrysanthemum is the ancient Greek name meaning golden flower; *cinerariæfolium* is from two Greek words meaning ash-colored leaves; *roseum* means rose-colored. Dalmatian insect powder is obtained from *C. cinerariæfolium*, a perennial herb indigenous to Dalmatia and Herzegovina, where it is also cultivated as well as in Africa, New York, and California and to a large extent in Japan. The Persian insect powder is derived from *C. roseum* and *C. Marschallii,* perennial herbs growing in the Caucasus regions, Armenia and northern Persia. The flowers are collected from two- to six-year-old plants, the flower heads being torn off by a combing machine and carefully dried and preserved. The finest and most powerful insect powder is obtained from the closed or only partly expanded flowers, provided they are properly dried and preserved.

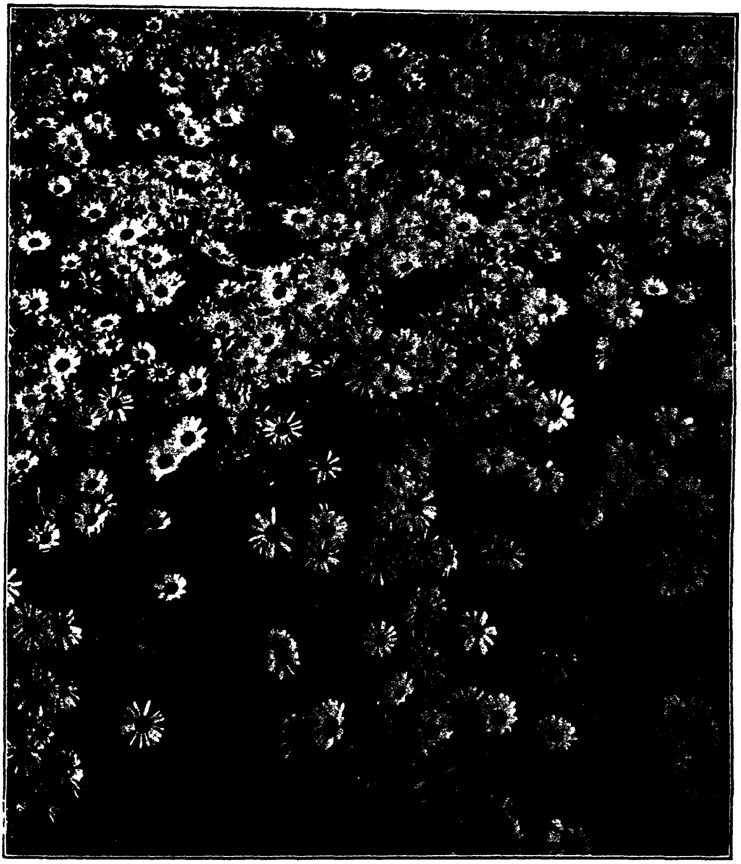


Fig. 358.—A portion of a plot of *Chrysanthemum cinerariifolium.* The flowers, which somewhat resemble the common white or field daisy, furnish the Dalmatian insect powder. (After Newcomb.)

Description.—See Figure 358. The flower-heads of Pyrethrum are hemispherical or subglobose and somewhat flattened, up to 20 mm. in diameter, and are composed of 30 or more yellowish white, straw-colored, weak yellowish orange, reddish or reddish purple ray florets and many yellowish orange to yellow disk florets on broadly conical or rounded receptacles. The ray florets are pistillate, possessing a strap-like corolla from 1 to 2 cm. in length and terminating in three short obtuse or rounded teeth. The disk florets are up to 7 mm. in length, are perfect and have 5-toothed tubular corollas borne on the achenes, the latter being 5- to 10-ribbed and provided with a short-toothed crown or pappus. The involucre is made up of 2 or 3 rows of bracts, the outer braots being lanceolate and distinctly keeled, somewhat hairy on the outer surface and smooth, shiny and weak yellowish orange on the inner surface. The inner bracts are spatulate, longer than the outer ones and have a white, dark red or reddish brown membranous margin. Stems are usually wanting, but if present are cylindrical, grayish or yellowish green, pubescent and show 9 to 12 prominent ribs.

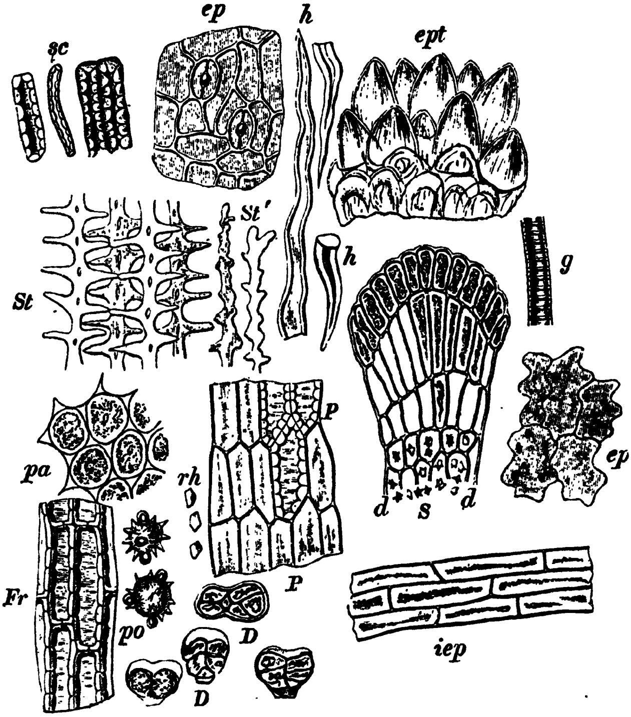


FIG. 359.—Pyrethrum (Insect flowers): *sc*, stone cells; *ep*, upper epidermis of a bract; *h*, *h*, non-glandular hairs of bracts; *ept*, papillæ on the upper surface of the ligulate corolla; *St*, *St'*, loose parenchyma of the ligulate corolla; *g*, a trachea of a bract with annular thickening; *S*, tooth of a tubular floret, some of the cells of which contain rosette aggregates of calcium oxalate; *ep'*, epidermis of the under surface of a ligulate corolla; *P*, section of pappus showing some of the lignified cells, some of which contain monoclinic prisms as shown at *rh*; *pa*, parenchyma of a bract; *Fr*, somewhat thickened, porous cells of the pericarp of the achenes; *D*, glandular hairs found on the wall of the ovary; *po*, pollen grains; *iep*, cells of the involucre between the bracts. (After Hanausek.)

Powder.—See Figure 359 and the National Formulary.

Constituents.—The two active constituents, toxic to insects are Pyrethrin I ($C_{21}H_{30}O_3$), and Pyrethrin II ($C_{22}H_{30}O_5$), both being esters of the alcohol Pyrethrolone. Other constituents include resin and volatile oil.

Adulterants.—Common field daisy or ox-eye daisy (*Chrysanthemum leucanthemum*), which can be detected microscopically by the nearly black secretion sacs, the irregular dark red fragments of the achene and the palisade cells comprising the costal tissue of the achene. It is stated that sometimes the entire stem with leaves is ground up with the flowers. Powdered insect flowers, which are bright yellow in color, usually have added to them powdered curcuma or chromate of lead.

Uses.—Powdered insect flowers is used as an insecticide. The most effective powder is said to be one 80 per cent of which will pass a 280 standard mesh sieve. Such powders are prepared by means of air-separation during the process of milling. Liquid preparations containing the toxic principles of insect flowers, kerosene and methylsalicylate, are being extensively employed in the form of sprays as fly and insect repellants.

Pyrethrum or Pellitory (U. S. P. 1820 to 1926) is the dried root of *Anacyclus pyrethrum*, a perennial herb indigenous to northern Africa and southern Europe, the commercial article coming from Algeria. The root is collected in autumn and dried.

The root is nearly cylindrical, slightly tapering, or broken into irregular pieces, 2.5 to 10 cm. in length, 3 to 20 mm. in diameter; externally dark brown, wrinkled and somewhat furrowed longitudinally, with few rootlets or rootlet scars; the crown is somewhat annulate from scars of bud-scales and sometimes tufted with coarse fibers of fibrovascular tissue or having long, soft-woolly, nearly straight, 1-celled hairs; the fracture is short and horny when dry, tough when damp; internally the bark is dark brown, with 2 circular rows of resin canals, 0.5 to 1 mm. in thickness and closely adhering to the light yellow, radiate, porous wood, in the medullary rays of which resin canals are also found; the odor is distinct and penetrating and the taste pungent, and acrid.

The powder is light to dark brown, and shows parenchymatous cells with irregular crystalloidal masses of inulin; nearly isodiametric stone cells, the contents of which are yellowish brown; reticulate, narrow tracheæ; a few sclerenchymatous fibers; the resin canals containing yellowish brown amorphous masses of a volatile oil and resin.

Pyrethrum contains an alkaloid, pyrethrine, which occurs in colorless, acicular crystals, has an intense pungent taste and is decomposed by alkalis into piperidine (a pungent principle occurring in black pepper) and pyrethric acid, a principle resembling piperic acid. Pyrethrum also contains a brown, acrid resin, two other acrid resins, a volatile oil and about 50 per cent of inulin.

Pyrethrum is a stimulant, a sialagogue, an irritant and a rubefacient.

German Pellitory, the root of *Anacyclus officinarum*, is smaller than pyrethrum; the bark contains but one row of secretion reservoirs, which are wanting in the medullary rays; and the roots contain tannin in addition to the constituents found in pyrethrum.

Absinthium, Common Wormwood or Absinthe (U. S. P. 1831 to 1905; N. F. 1916 to 1926) consists of the dried leaves and flowering tops of *Artemisia absinthium*, a shrubby perennial herb, growing in waste places in the northern United States and Canada. It is cultivated in Europe, northern Africa, New York, Michigan, Nebraska and Wisconsin. The volatile oil is used in the preparation of the French Absinthe. The leaves and flowering tops are gathered during the summer or early fall, carefully dried and preserved.

The leaves are from 5 to 12 cm. in length, 2- to 3-pinnately divided, the lobes being obovate or lanceolate, entire or toothed, the lower being long petiolate; the heads are greenish yellow, hemispherical or ovoid and arranged in panicles, the involucral scales being in two series, the inner linear and having membranous margins; the florets are all tubular, the outer ones sometimes being neutral. The herb is aromatic and very bitter.

Non-glandular hairs of two kinds are present: (*a*) Unicellular, very long; (*b*) T-hairs consisting of a 1- to 4-celled stalk, bearing a single horizontal cell at the summit; glandular hairs having a 1- or 2-celled stalk and a glandular summit consisting of 4 to 8 cells; the pollen grains are spheroidal, about 30 microns in diameter, nearly smooth, and having 3 pores; calcium oxalate is in rosette aggregates about 10 microns in diameter; the tracheæ are spiral or have simple pores and associated with slightly thickened, lignified, porous wood fibers.

The fresh drug contains about 0.5 per cent of a volatile oil which is of a dark green or blue color, has a bitter, persistent taste but not the pleasant odor of the plant, and consists of *d*-thumone (absinthol), thujyl alcohol, free and combined with acetic, isovaleric and palmitic acids, phellandrene and cadinene; also a bitter glucosidal principle, absinthiin, which forms white prisms and yields on hydrolysis a volatile oil; a resin; starch; tannin; succinic acid; potassium succinate and about 10 per cent of natural ash with about 1.3 per cent of acid-insoluble ash.

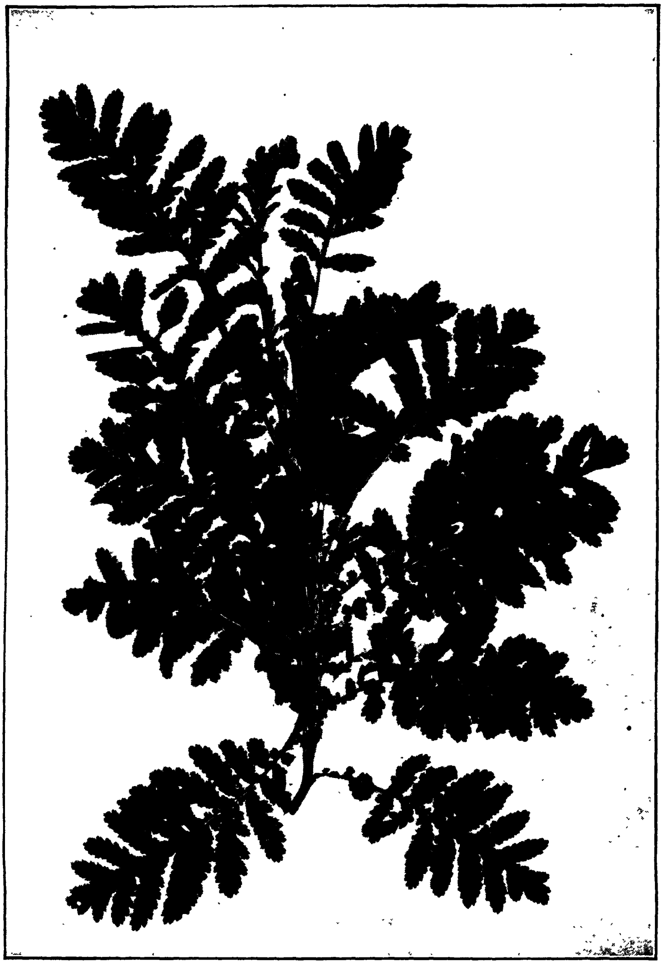


Fig. 360.—Branch of Tansy (*Tanacetum vulgare*) showing closely alternating, deeply pinnatifid or pinnately divided leaves, the divisions being linear, oblong and variously lobed and incised.

Absinthium is used as a tonic, a stimulant, an anthelmintic and a febrifuge. Average dose, 2 gm.

Achillea, Yarrow or Milfoil (U. S. P. 1863 to 1882) consists of the dried leaves and flowering tops of *Achillea millefolium*, a common roadside weed, naturalized from Europe and Asia, and contains about 0.1 per cent of a dark blue volatile oil with a strongly aromatic odor and a small amount of a bitter alkaloid, achilleine. The roots of yarrow, on the other hand, yield a volatile oil with a valerian-like odor.

Achillea is used as a tonic, a stimulant and an emmenagogue.

Achillea nobilis of Europe contains an oil resembling that of yarrow, but is of finer quality and has a spice-like taste. *Achillea moschata*, an alpine plant of Europe, yields three alkaloids and a volatile oil containing cineol and is used in Italy in the preparation of the liquor, "Esprit d'Iva." *Achillea tanacetifolia* yields a blue volatile oil having the odor of tansy.

Tanacetum or Tansy (U. S. P. 1820 to 1905) consists of the dried leaves and flowering tops of *Tanacetum vulgare*, a perennial aromatic herb (Fig. 360), indigenous to Europe, extensively cultivated and naturalized in the United States. The leaves are large and pinnately divided, and the flowers, both tubular and ligulate, are yellow, the heads being in terminal corymbs.

The powder is yellowish green and shows a few 4- to 5-celled, non-glandular hairs, about 150 microns in length, the individual cells being somewhat oblong and with yellowish brown contents; glandular hairs on achenes with short stalk and large, ellipsoidal head; involucral bracts with a row of transparent marginal cells and a central portion with narrow, thick-walled, libriform cells having numerous simple pores; spheroidal, thick-walled, pollen grains with numerous spinose, centrifugal projections; narrow tracheæ having scalariform and reticulate perforations or bordered pores; thin-walled sclerenchymatous fibers free from pores.

Tansy yields from 0.1 to 0.3 per cent of a volatile oil, consisting of thujone, borneol and camphor; and also three resins.

Tansy is used as a stimulant, an emmenagogue and an anthelmintic.

ERIGERON

Erigeron Heterophyllum, Daisy Fleabane or Sweet Scabious (U. S. P. 1831 to 1863; as Erigeron, 1863 to 1882) consists of the leaves and tops of *Erigeron heterophyllum* Muhlenberg.

Erigeron Philadelphicum or Philadelphia Fleabane (U. S. P. 1831 to 1863; as Erigeron, 1863 to 1882) consists of the leaves and tops of *Erigeron philadelphicus* Linné.

Erigeron or Fleabane (U. S. P. 1863 to 1882); see Erigeron Heterophyllum and Erigeron Philadelphicum.

Erigeron Canadense or Canada Fleabane (U. S. P. 1820 to 1882) consists of the leaves and flowering tops of *Erigeron canadense* Linné.

Oleum Erigerontis, Oil of Erigeron, Oil of Canada Erigeron or Oil of Fleabane (U. S. P. 1863 to 1916) is the volatile oil distilled from the fresh flowering herb of *Erigeron canadense* Linné.

Erigeron, from the Greek, means spring and old man, and refers to the hoariness of some species in the early spring. The plants are annual or biennial (*E. philadelphicus* perennial), and are common weeds in many parts of the United States and Canada east of the Mississippi River. They prefer moist, good soil. The leaves are alternate or basal and, with the stems, usually are hairy. The flower-heads are relatively small and, especially on *E. canadense*, are numerous. Odor is aromatic and taste is bitterish, acrid and somewhat astringent, *E. canadense* being the strongest.

The plants contain volatile oil, that from *E. canadense* much more abundant; some resin; a little tannin; mucilage, etc.; neither glucosides nor alkaloids have been noted.

The drugs are stimulant and diuretic; the volatile oil is much the strongest, having been used to quicken uterine contractions. Dose of the herbs, 2 gm.; of the oil, 0.3 cc.

Farfara, Tussilago or Coltsfoot (N. F. 1916 to 1936) is the dried leaf of *Tussilago farfara*, a low perennial or acaulescent herb, indigenous to Europe and growing in wet places and along roadsides in the northern United States and Canada. The variegated variety, the leaves of which have a creamy white margin, is a common ornamental plant, thriving in shady places. The leaves are gathered in June and July, after the flowering of the plant, carefully dried and preserved.

The leaves usually occur in broken pieces; when whole they are ovate-reniform, long petiolate, from 8 to 15 cm. in length with an acute apex, a cordate base, angulate lobes, and dentate margin, having reddish brown teeth; a dark green and glabrous ventral surface; a white tomentose dorsal surface having 5 to 9 prominent palmate veins; the odor is slight, and the taste mucilaginous and slightly bitter.

The powder is yellowish green and shows numerous multicellular, non-branching hairs, usually curved and twisted together, the terminal cells much elongated, and sometimes with spiral bands; broadly elliptical stomata up to 54 microns in length and associated with finely striated epidermal cells with wavy vertical walls; beneath each stoma is a 6-sided characteristic intercellular space; few non-porous fibers with walls from 6 to 12 microns in thickness.

Coltsfoot contains an acrid volatile oil, a bitter glucoside, gallic acid, albuminous substances, a caoutchouc-like substance, resin and tannin. Well-cleaned leaves yield about 10 per cent of total ash and about 0.25 per cent of acid-insoluble ash; commercial drug from 1.5 to 3.5 per cent of acid-insoluble ash. The drug yields from 14 to 16 per cent of non-volatile extractive when exhausted with diluted alcohol. Moldy or decomposed leaves from partially dried drugs causes inferiority. Old, dead leaves are sometimes present, and occasionally an excess of sand.

Coltsfoot is a demulcent. It is also used as an expectorant.

Senecio, Golden Senecio, Ragwort or Life Root (N. F. 1916 to 1936) is the dried overground plant of *Senecio aureus*, a perennial herb, growing in swamps and wet meadows throughout the northern and central United States.

The leaves and flowering tops are gathered in the early summer and carefully dried.

The drug consists of a group of basal leaves and a leafy, flowering scape. The basal leaves are orbicular or oblong, long petiolate, the lamina from 1 to 6 cm. in length and 1 to 5 cm. in breadth, with a rounded summit, acute or cordate base, a crenate-dentate margin; both surfaces olive-green or purplish green, considerably wrinkled, glabrous, the midvein and lower veins of the first order prominent; the petioles are from 3 to 8 cm. in length, having 8 to 10 prominent ribs, light brown and frequently covered at the base with soft, woolly hairs. The flower stalk is from 15 to 40 cm. in length, having 8 to 10 prominent ribs, olive-green when young, usually covered with soft woolly hairs, which are easily detachable, leaving the stems glabrous. The stem leaves are alternate, the upper sessile, the lower petiolate, having a lanceolate outline and usually laciniate-pinnatifid. The flowers are in open corymbs, the heads having slender peduncles which vary from 3 to 7 cm. in length; involucral scales, linear, erect-connivent; ray florets 8 to 12, having golden-yellow ligulate corollas; tubular florets yellow and perfect; achenes hairy and having a white pappus, about 6 mm. in length; the odor is distinct, aromatic and the taste acrid and somewhat bitter and pungent.

The epidermal cells have undulate walls, the stomata being narrowly elliptical, about 30 microns in length, with the neighbor cells transverse to the pore; transverse sections of the petiole are somewhat arrow-shaped, showing 2 to 4 layers of subepidermal collenchyma and from 8 to 10 fibrovascular bundles; the stems show a strong development of collenchyma at the ribs and the fibrovascular bundles are arranged in a closed ring, each being surrounded by a strong development of fibers; the pith is hollow. The woolly hairs of the stems and petioles are very long, thin-walled and up to 40 microns in width; the non-glandular hairs on the leaves are few, uniseriate, about 250 microns in length and consisting of 5 or 6 short, cylindrical cells, having thin walls and an oily content; the achenes are covered with club-shaped or spatulate hairs, about 180 microns in length and finely, transversely or obliquely, striate; the pappus is multicellular, having at the jointed portions, short, sharp-pointed cells.

Kelly and Lynn found 0.1 per cent of volatile oil and about 8 per cent of inulin, but no evidence of either alkaloids or glucosides. Senecio is said to be a stimulant, a diuretic and an emmenagogue; no evidence has, however, been found of its having any uterine effect.

Senecio jacobæa, indigenous to Europe and Asia and localized to some extent in the New England States and Canada, and *S. vulgaris* somewhat resemble *Senecio aureus*. They are said to contain a mixture of alkaloids, senecionine and senecine; a volatile oil; 0.98 per cent of a fatty substance, soluble in ether; 0.88 per cent of a mixture of fatty acids; and 0.8 per cent of ash.

Lactuca Elongata or Wild Lettuce (U. S. P. 1820 to 1851) consists of the flowering herb of *Lactuca virosa* Linné.

Lactucarium (U. S. P. 1820 to 1926) is the dried milk juice of *Lactuca virosa* and other species of *Lactuca*, biennial herbs largely indigenous to central and southern Europe and cultivated in France, England and Germany, certain species being more or less naturalized in the United States.

Lactucarium is obtained by cutting off the tops of the stems; when the latex which exudes is partially hardened, it is collected and dried in hemispherical earthen cups until it can be cut into pieces, which are usually four in number, these being further dried.

It occurs in irregular, angular pieces or quadrangular sections, one surface of which is convex; externally dull reddish or grayish brown; fracture tough, waxy; internally light brown or yellowish, somewhat porous; odor distinct, opium-like; taste bitter.

Lactucarium is partly soluble in alcohol and in ether and about 50 per cent soluble in water, but the solution should not give a reaction for starch.

The powder is grayish brown to dark brown and consists of irregular and rather angular masses; with alkalis they become reddish brown and then a dirty brown; with sulfuric acid they are but slightly affected.

The drug contains three bitter principles: lactucin, which occurs in white rhombic prisms that are sparingly soluble in water; lactuco-picrin, a brown, amorphous, very bitter principle which is readily soluble in water and alcohol; and lactucic acid, a yellow, very bitter substance crystallizing with difficulty and colored red by alkalis. The drug also contains about 50 per cent of a colorless, odorless and tasteless crystalline principle, lactucerin (lactucon); β- and α-lactucerol in the form of acetates; volatile oil; mannitol; organic acids, as citric, malic and oxalic and from 6.5 to 10 per cent of ash, nearly all of which is acid-insoluble.

A mydriatic alkaloid has been found in *Lactuca virosa* and in *L. muralis*.

Lactucarium is said to have some hypnotic effect; if so, it is very feeble. It is generally stated to be a sedative, a diuretic and an expectorant.

ALLERGENIC PREPARATIONS

Pollinosis, commonly called hay-fever, is an allergic manifestation produced in hypersensitive individuals by the pollen grains of certain plants. These allergenic pollens are wind-borne and sufficiently light to be carried great distances. Not all wind-borne pollens are capable of producing allergic response. The chief factor in pollen allergy is the ability of pollen grains to stimulate an antigen-antibody response in susceptible persons.

The most popular method (Gravity Method) of determining wind-borne pollens is by the periodic exposure of microscopic slides coated with glycerin, petrolatum, or glycerin jelly to atmospheric currents for twenty-four hours. Protection from rain must be provided. The slide is then examined microscopically to identify and count the pollen grains which have lodged on the adhesive surface. Pollen grains vary greatly in size and appearance. Many are smooth, others have barbs or furrows, and still others are spiny. It is possible to identify plant species by close observation of their pollen. The average number of each kind of allergenic pollen grains per slide at each daily or periodic exposure is used as a basis for comparison in each locality. The number of grains per square centimeter of slides can be related to the number of grains per cubic yard of air by the use of the Scheppegrell formula as revised by Cocke. Daily atmospheric pollen counts are determined during the pollen season for the larger cities of the United States and for many cities in Central and South America. Other methods are claimed by some investigators to be more efficient: The Open Dish Method; Well's Air Centrifuge; The Aerosol Collector, which is an air filter devised by Erdtman.

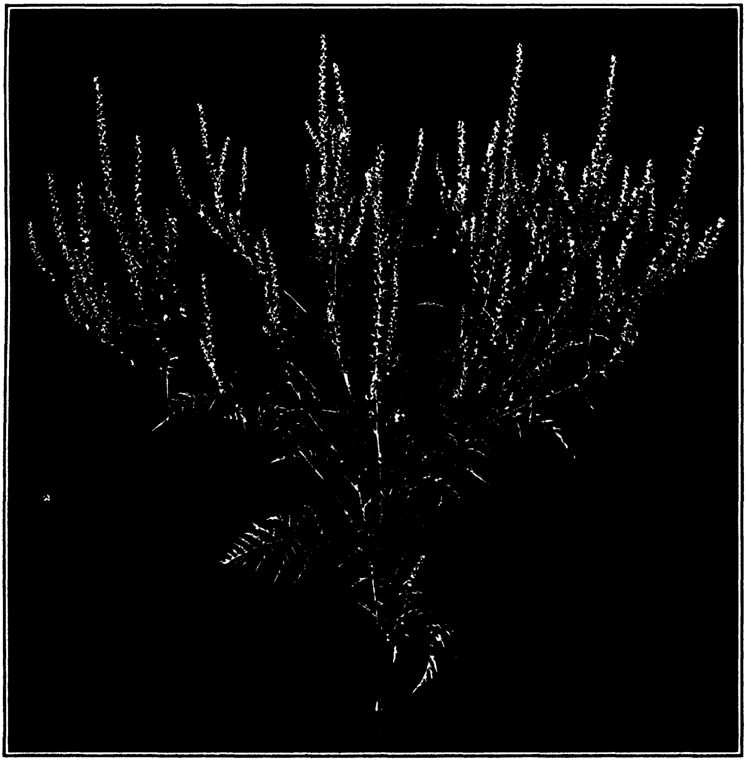


FIG. 361.—Common or Short Ragweed, *Ambrosia artemisiæfolia*, the most important cause of hay-fever. (Photo, courtesy of Abbott Laboratories.)

Three seasons of pollinosis are recognized in most of the United States: spring hay-fever caused by tree pollens; early summer hay-fever (commonly called rose-fever) produced by grass pollens; and late summer or fall hay-fever due to the pollens of ragweed and other weeds. The flowering seasons of these plants overlap in the southern and southwestern states, and it is difficult to apply a descriptive term for seasonal pollinosis.

The elms (*Ulmus*), the maples (*Acer*), the oaks (*Quercus*), the walnuts (*Juglans*), the birches (*Betula*), the poplars (*Populus*), the alders (*Alnus*), the willows (*Salix*), the hackberries (*Celtis*), and many other trees flower early in the spring.

Bermuda grass (*Cynodon dactylon* [L.] Pers.), Johnson grass (*Sorghum halepense* [L.] Pers.), orchard grass (*Dactylis glomerata* L.), sweet vernal grass (*Anthoxanthum odoratum* L.), red top (*Agrostis alba* L.), timothy (*Phleum pratense* L.), and June grass (*Poa pratensis* L.) are a few of the many grass pollens capable of causing an allergic response. Certain members of the *Chenopodiaceæ*, *Plantaginaceæ*, *Polygonaceæ*, *Amaranthaceæ*, *Compositæ*, and other families develop their flowers from mid-summer to the end of the growing season and produce allergenic pollens.

Of the *Compositæ*, the ragweed genus (*Ambrosia*) is responsible for approximately 90 per cent of the pollen allergy in the United States. Tall ragweed, giant ragweed, or great ragweed (*Ambrosia trifida* L.) is a coarse annual which sometimes grows to a height of 15 feet. The staminate flowers are borne in terminal spikes at the base of which are the pistillate flowers. The leaves are opposite and long-petioled. The lower leaves are more uniformly three-lobed than the upper.

Dwarf ragweed, common ragweed, short ragweed, or hogweed is known by the name *Ambrosia artemisiifolia* L., although recently taxonomists have suggested that this plant is synonymous with *Ambrosia elatior* L. Short ragweed is a much-branched annual which occasionally grows 6 feet high. It is characterized by its numerous staminate spikes and by its fern-like leaves which are once- or twice-pinnatifid. Short ragweed, as well as tall ragweed, occurs chiefly in the northeastern, middle Atlantic, and central states. Two other important species are the southern ragweed (*A. bidentata* Michx.) and the western ragweed (*A. psilostachya* DC.). Other fall-blooming genera are false ragweed (*Franseria*), the prairie ragweeds (*Iva, Cyclachæna*), cocklebur (*Xanthium*), and wormwood (*Artemisia*) which produce pollens of equal potency.

Pollen may be collected from plants in the following manner: cut the stems 12 to 18 inches below the flowering heads; place them in a pan of water so that the heads hang over the edge; collect the pollen on glazed paper placed beneath the heads. The following morning considerable pollen will have been shed onto the paper. An equal or larger yield will be obtained on the second morning and a smaller one on the third morning. Finally, the plants are shaken vigorously to remove the remaining ripe pollen, and then are discarded.

The dried pollen is defatted with ether and extracted with saline solution. Glycerin or dextrose is added to serve as a stabilizer in the preservation of the extract. The resulting solution is filtered by suction or pressure to render it sterile, and is then assayed for the number of units of nitrogen per cc. The finished extract is marketed in vials with the potency indicated on the label. Individual doses may be supplied ready for dilution and injection.

Recent investigators have indicated that water-soluble proteins of pollen grains are the allergenic factors. When the individual absorbs the protein of a pollen he becomes hypersensitive to that protein. The subsequent absorption of some of the same protein, even though in smaller amounts, creates a sudden reaction or shock accompanied by urticaria, lacrimation, sneezing, or inflammation of the sinus membranes. Susceptibility is determined by skin tests. An extract of the pollen is injected into the subcutaneous layers of the arm and the resulting reaction is compared with a control spot. A wheal or redness signifies a positive reaction and indicates that the person is allergic to the pollen and should be desensitized.

Treatment is co-seasonal although desensitization is best accomplished by pre-seasonal or annual treatment. Extreme care must be used in determining the dosage for each patient. Sensitivity varies greatly and an overdose may cause disagreeable or alarming symptoms or even death.

Investigations have proved that the spores of molds, mildews, and other fungi are also important causes of allergy. Mold extracts, like pollen extracts, are used to ascertain susceptibility and to produce desensitization. Pollens, mold spores, dander, epidermis, and dusts are inhalant allergens. Contactant allergens include wool, feathers, hair, poison ivy, and poison sumac. The latter are discussed on page 405. Ingestant allergens such as strawberries, tomatoes, eggs, cheese, wheat, and other protein foods have been extracted. These extracts are used chiefly as diagnostic agents to determine susceptibility.

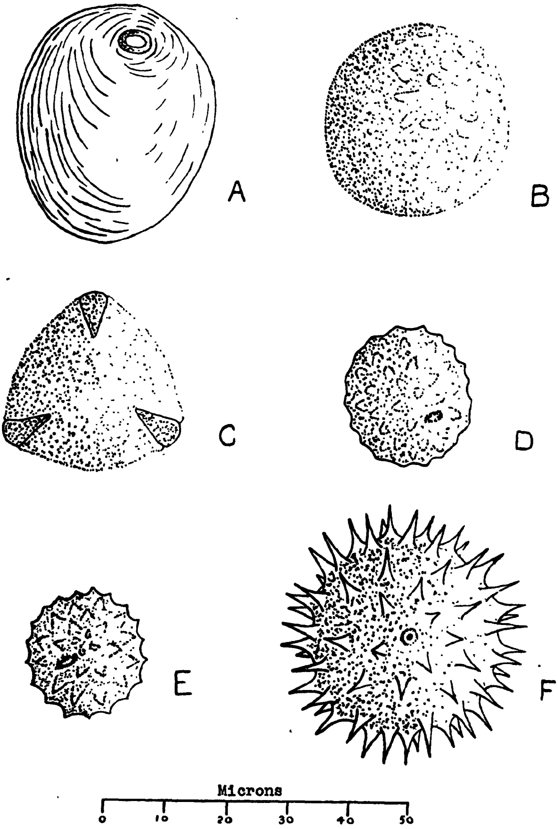


FIG. 362.—Pollen grains: *A*, Sweet vernal grass. *B*, Cottonwood. *C*, White oak. *D*, Short ragweed. *E*, Giant ragweed. *F*, Goldenrod.

ANIMAL DRUGS

THE taxonomy of animals is similar to that of plants. The animal kingdom is divided into sub-kingdoms or phyla and these in turn into classes, orders, families, genera and species. Since the number of drugs derived from animals is much smaller than the number derived from plants, only a very brief survey of some of the phyla will be presented here. Those phyla yielding no drugs will be omitted.

Protozoa are 1-celled animals such as the *Amœba, Paramœcium* and *Vorticella.* The order *Foraminifera* contains animals the shells of which comprise the natural chalk deposits of Cornwall and other parts of the world. While these shells are composed largely of calcium carbonate they also contain more or less silica, aluminum, magnesium and organic matter. **Creta Præparata, Prepared Chalk,** U. S. P. 1820 to date is obtained by elutriation from this native chalk.

Porifera are animals having many similar cells arranged about a common cavity, the food entering the body through numerous openings. To this phyllum belong the sponges.

Spongia or Sponge, and Spongia Usta or Burnt Sponge (U. S. P. 1820 to 1863) consist of the fibrous framework of *Espongia officinalis.* Sponges grow in the sea, attached to rocks and are very often planted in beds for cultivation. When full grown the sponges are torn from the rocks and buried in the sand to disintegrate the gelatinous animal matter which is removed by washing. There are several commercial varieties, among which the following may be mentioned: (1) Mediterranean, Turkey; (2) Zimocca (coast of Greece); (3) Bathing (coast of North Africa); (4) Sheep's Wool (coast of Florida and the Bahamas). Sponges are used mechanically for cleaning and washing and for absorbing liquids. They have been used in dilating cavities (sponge tents) and as pessaries in dysmenorrhea.

Cœlenterata are animals having hollow cylindrical bodies with one opening, the mouth. To this phylum belong the hydras, hydroids, jelly-fish, corals and the sea-anemones. The corals are animals having a calcareous skeleton which is more or less branched. It is on these branches that the individual animals are found in tube-like apertures. The calcareous skeleton **(coral)** has been used to some extent in tooth-powders as an antacid.

Platyhelminthes is the phylum containing the tapeworms and the phylum **Nemathelminthes** the threadworms, trichina, hookworm, etc.; all these are of interest as parasites of the human body.

Annulata are worm-like animals. To this phylum belong the earthworm and the leeches.

Three **leeches** have been used in medicine: the Speckled, Green or Gray Leech (*Hirudo medicinalis*), a native of northern and central Europe; the Australian or Five-striped Leech (*Hirudo quinquestriata*) and the American Leech (*Hirudo decora*). Leeches are from 6 to 12 cm. long, dorsiventrally flattened and show about 100 rings or annulations. The anterior end has a cup-like sucker in the center of which is the mouth with three radiating jaws provided with many chitinous teeth with which the leech produces its characteristic triradiate bite.

Leeches live in ponds, marshes and running streams in practically all temperate climates. They should be kept in water in jars which are tightly covered with a linen cloth. The water should be changed once or twice each week and occasionally gravel or sand may be added so that the animals may clean themselves of the slime which accumulates on their bodies.

Although used much less than formerly, leeches are still employed to relieve local congestions or inflammations, especially where the vessels have been ruptured and the blood diffused into the connective tissue. The point at which the application is to be made should be cleansed and freed from hair and if it be advisable to localize the bite a piece of moistened filter paper with a small hole may first be applied to the area. Leeches withdraw from 5 to 10 cc. of blood and may be removed by sprinkling them with salt. The bite continues to bleed for a considerable time, due to the fact that the salivary glands of the leech produce a substance known as *hirudin* which retards the coagulation of the blood. The use of the same leech for different patients should be discouraged due to the danger of carrying infection.

Mollusca are soft-bodied animals often enclosed in hard shells. To this phylum belong clams, snails, the nautilus, the squid and the cuttlefishes.

Os Sepiæ or Cuttlefish Bone is the internal shell of *Sepia officinalis*, a 10-armed squid closely related to the octopus (8-armed). The animals inhabit the Atlantic and Indian Oceans and the Mediterranean. The calcareous skeleton or shell rises to the surface of the sea after the death of the animal and may be collected. Cuttlefish bones are quite common on the shores of Europe and the Indian Ocean. In common with the other squids the cuttlefish possesses an ink gland, and from this is obtained the dye used in water colors and known as **sepia**, Cuttlefish bones are oblong-ovate and more or less biconvex, up to 25 cm. long, 7.5 cm. wide and 2 cm. thick. The outer portion is hard but the inner part is porous and friable. Cuttlefish bone contains from 80 to 85 per cent of calcium carbonate and has been used as an antacid; in tooth and polishing powders; for caged birds to sharpen their bills against; and as an abrasive.

Oyster-Shell (U. S. P. 1831 to 1882) is the inner white layer of the shell of the oyster (*Ostrea virginiana* and other species of *Ostrea*). Oysters are bivalves which inhabit the shores of the Atlantic and the Indian Oceans. In the preparation of **Prepared Oyster Shell** (U. S. P. 1831 to 1882) for medicinal use, the shells are boiled, and the outer layer removed; then the inner layer is powdered, the coarser particles being separated by elutriation. Oyster-shell consists mostly of calcium carbonate (88 to 98 per cent) and has been used as an antacid.

Arthropoda are animals having segmented bodies and jointed appendages. To this phylum belong the insects (see below).

Vertebrata or **Chordata** are animals having a backbone made up of parts called vertebræ. To this phylum belong fishes, frogs, turtles, snakes, birds, horses and man. Older classifications divided the animal kingdom into two sub-kingdoms, *Invertebrata*, including the previously discussed groups, and the *Vertebrata*.

As the insects and vertebrates (see page 662) yield a number of important drugs, these groups will be discussed at greater length.

CLASS INSECTA

This class includes those small animals which have 1 pair of antennæ, 3 pairs of mouth organs, 6 legs, 1 or 2 pairs of wings and breathe air by means of tracheæ extending from openings, called spiracles, on the sides of the body. The bodies of the insects are divisible into three distinct parts; the head, the thorax and the abdomen. Examples of the group are grasshoppers, dragon-flies, moths, beetles, flies, etc.

ORDER HEMIPTERA, FAMILY COCCIDÆ

This order includes insects having suctorial mouth parts. The wings are two or four in number and are usually membranous. The insects feed on plant juices and animal blood. The group includes the squash-bug, bed-bug, plant lice and the scale insects.

The *Coccidæ* include the scale insects and bugs which are injurious to plants. The members of the family differ greatly from the members of other families in this order and also often show considerable variation among themselves. The males undergo complete metamorphosis and possess only one pair of wings. The female has no mouth parts and is always devoid of wings. It is usually covered with scales which form a protective case.

COCHINEAL

Cochineal or Coccus (U. S. P. 1831 to date; in test solution, U. S. P. 1894 to 1936; N. F. 1936 to date) consists of the dried female insect, *Coccus cacti* Linné, enclosing the young larvæ. The generic name *Coccus* is from the Greek *Kokkos*, meaning a grain or berry and refers to the appearance of the insect; *cacti* is from the Greek *Kaktos*, meaning a prickly plant, the insects being cultivated on various species of cactus.

The cochineal insect feeds upon various species of the *Cactaceæ*, more especially the Nopal plant, *Nopalea cochenillifer* (*Opuntia coccinellifera*), a native of Mexico and Peru. It has spread in Central and South America and has been introduced into the West Indies, East Indies, Canary Islands, southern Spain and Algeria and is said to be found in Florida and California.

The female insect is without wings, about 2 mm. in length and consists of from 9 to 12 segments. It is somewhat globular, becoming later distinctly ovoid. In general appearance, as it creeps over the cactus stems, it is convex on the upper (dorsal) surface and somewhat flattened or concave below. It is covered with a protective secretion or wax which is formed as a glandular secretion by the "wax pores" (Fig. 363, *w*), and wax hairs. The antennæ are rather short, consisting of 8 parts. The thread-like beak or proboscis, forming a sucking apparatus, is very fully developed. There are 3 pairs of legs and projecting from the posterior portion of the abdomen there are 2 short hairs or bristles. The female insect after fecundation grows larger as the young larvæ develop, becoming eventually about twice her original size. The cochineal of commerce consists of the females which are removed by the planters from the Nopal plants. They are then subjected to steam or hot water and dried, or they may be dried by direct heat.

DESCRIPTION.—It is concavo-convex, about 5 mm. in length, dark garnet in color. The mouth part of the insect with a more or less developed beak or rostrum is always present, the beak sometimes being extended and recurved in an elliptical form in the direction of the abdomen. One or both of the antennæ are frequently present, showing 5 to 7 parts. The joints of the legs are usually more or less detached, the point of insertion usually being indicated only by large yellowish brown elliptical scars. Between each of the legs on both sides are situated 2 distinct pores, which resemble in form and color the point of attachment of the legs and which are respiration canals. In the abdominal region, which is very large, the larvæ are borne. These are usually seen to be in several stages of development (Figs. 363, 364 and 365).

The following method is useful in destroying the coloring matter, thus rendering it possible to study the cochineal insect; 10 gm. of commercial cochineal is macerated with 100 cc. of water containing 2 or 3 per cent of an alkali. The mixture is allowed to stand for an hour or so and then is poured over a piece of wire gauze. The insects remain on the gauze and are then washed with a few

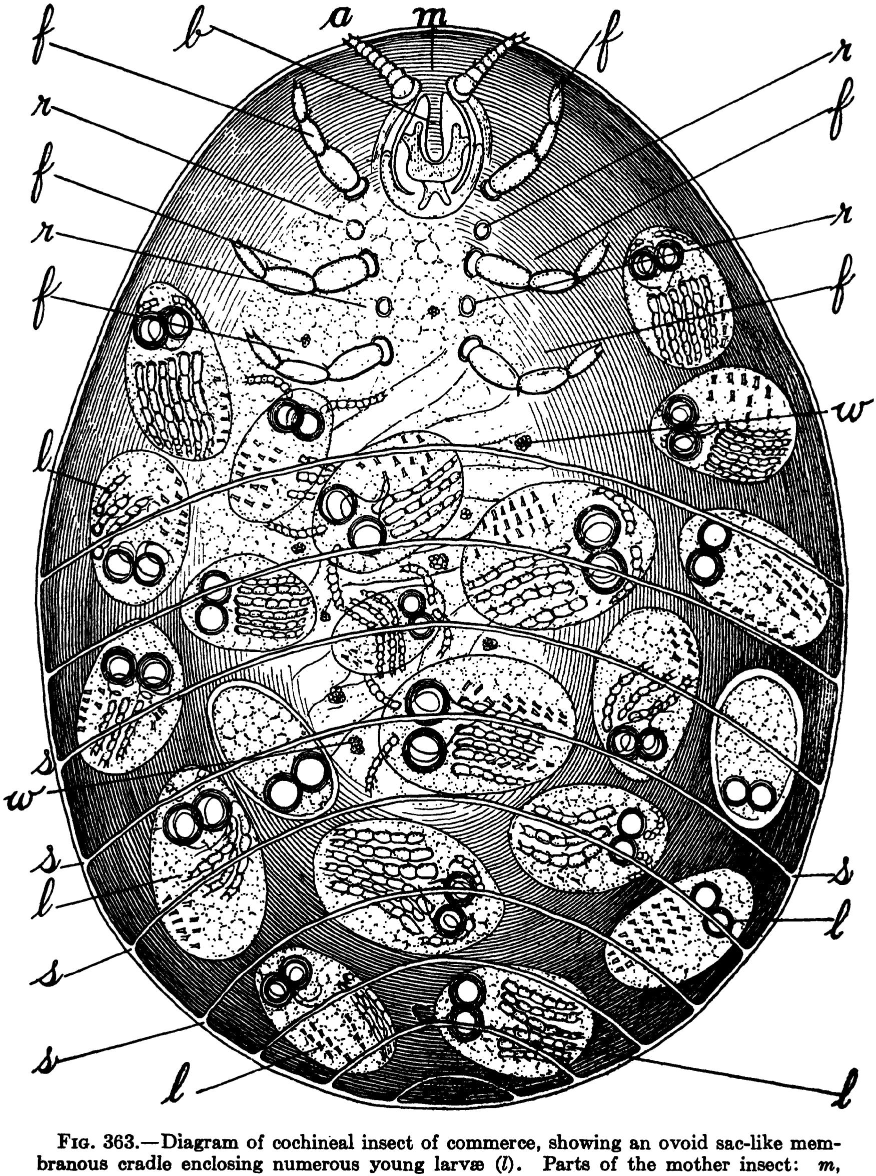


FIG. 363.—Diagram of cochineal insect of commerce, showing an ovoid sac-like membranous cradle enclosing numerous young larvæ (*l*). Parts of the mother insect: *m*, mouth part; *b*, beak or proboscis; *a*, antennæ; *f*, three pairs of legs; *r*, respiration channels or breathing pores; *s*, segments in abdominal region; *w*, wax-pores.

liters of water. The insects, from which the coloring matter has been partly removed, are then transferred to 150 cc. of hydrogen peroxide solution and allowed to stand for a few hours with occasional gentle stirring. The mixture is again transferred to the gauze, the excess of hydrogen peroxide washed off and the insects then transferred to a weak alkali solution in which they are macerated for six or eight hours. The mixture is poured upon the wire gauze

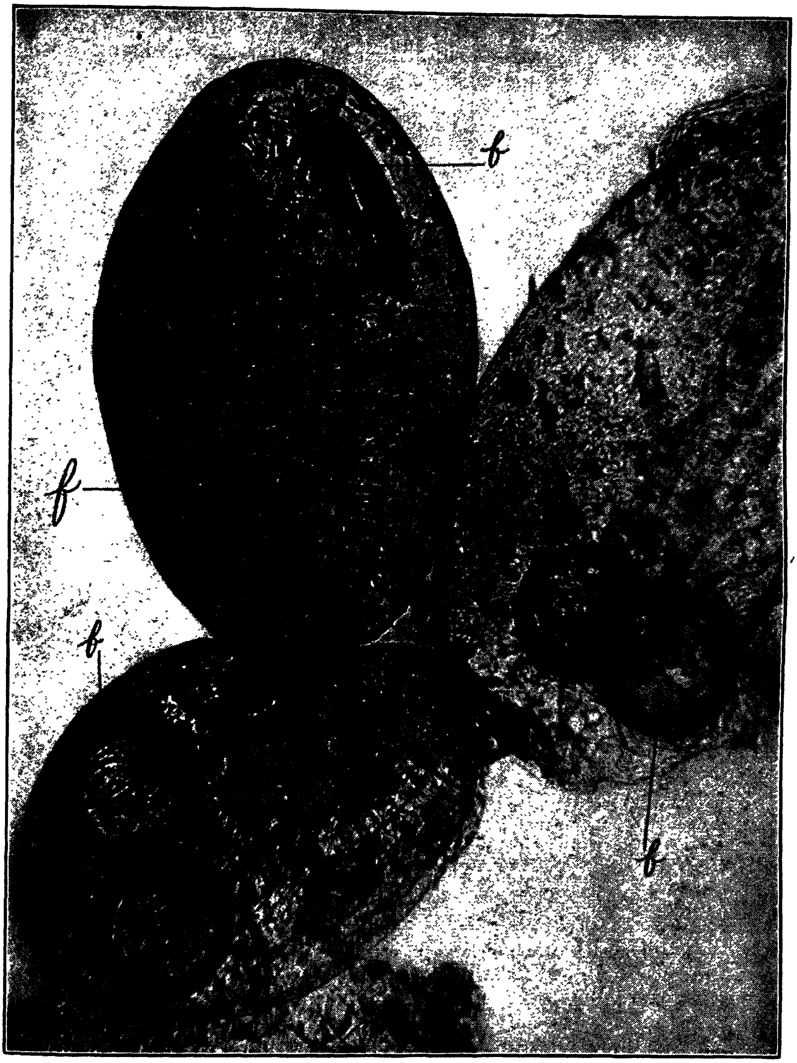


FIG. 364.—Photomicrograph of several of the numerous larvæ found in the mother insect and in which are to be seen the characteristic beaks (*b*); and the three pairs of legs (*f*) still enclosed in the sac-like membrane of the larva.

and washed with water until the filtrate runs practically colorless. The insects on the gauze are then transferred to dilute alcohol to which a few drops of hydrochloric acid have been added. This now renders them translucent and ready for microscopic study. They may be mounted in chloral T.S. and examined.

CONSTITUENTS.—From 9 to 10 per cent of a glucosidal coloring principle, carminic acid (carmine red). It is methyldioxy-naphthoquinone and forms crystals, which are very soluble in water, alcohol and ammonia, partly soluble in ether, and insoluble in fixed and volatile oils. Cochineal also contains 0.5 to 4.2 per cent of a wax, coccerin; from 1.5 to 2 per cent of myristin; from 4 to 6 per cent of a mixture of fats and fatty acids; total ash, from 0.5 to 6 per cent, with about 0.5 per cent insoluble in diluted hydrochloric acid.

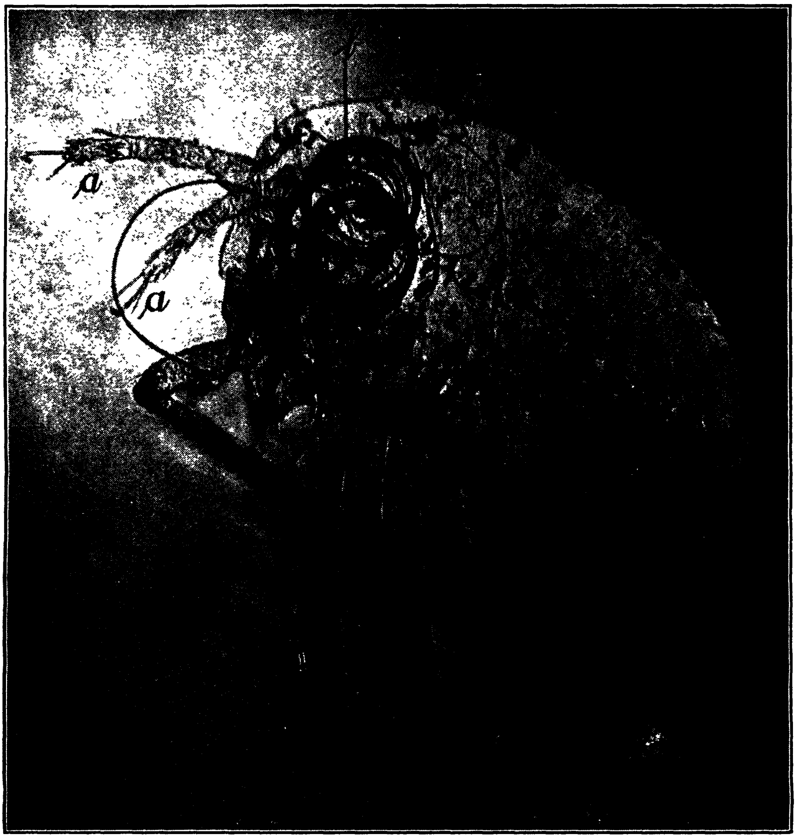


FIG. 365.—Photomicrograph of larva in cochineal insect of commerce showing: outspreading antennæ (*a*) and feet (*f*); the characteristic beak or proboscis (*b*); and wax-hairs on the body (*h*).

TESTS.—The red color of dilute aqueous solutions of cochineal is changed to purple by alkalis and to light orange by acids.

When whole cochineal is macerated in water, no insoluble powder separates from the mixture (inorganic matter used for weighting).

USE.—The principal use of coccus is as a coloring agent.

COMMERCIAL GRADES.—There is considerable variation in the quality of the commercial article. The most valuable variety is known as "Madres" and represents the first brood of the season. At one time Honduras shipped the best commercial article. At the present time, the greater quantity comes from Teneriffe, one of the Canary Islands.

According to the fancy of the broker or exporter, several grades of cochineal are recognized. Broadly speaking, the terms "silver grain," "black grain" and "granilla" are used, but there are intermediate qualities variously designated as gray, black-gray, silver-gray, silver-black, rosy black, red and foxy, and these again may be qualified by the terms fair, bold, fine and so forth. The commercial variety known as "granilla" represents the smaller females in which the larvæ usually show but a very slight development.

"Silver grain" is prepared by drying the insects in trays in the sun, or in an oven at a moderate temperature (about 65° C.) for four or five hours and subsequently in the sun so that the waxy substance is not melted and the color is whitish with a silvery sheen. If they are dried at a higher temperature than 106° C., the melting-point of the wax, on hot iron plates, the black grain is the result. The red tint of the rosy black is said to be produced if they are put in bags and dipped in boiling water to kill them before drying and that of the foxy silvery grain is produced by sifting the insects when not perfectly dry so that some of the coloring matter tinges the surface. The black grain usually obtains a higher price than the silver grain. Both the black and silver grain are sometimes adulterated to meet the demand for a cheap article. The black grain is sometimes met with having the concave side filled with grains of a magnetic iron sand. The silver grain is said to be weighted with sulfate of barium or carbonate of lead and the very white appearance is given by powdered talc or other white powder.

Carmine (N. F. 1916 to date; as a coloring agent U. S. P. 1916 to 1926) is the aluminum lake of the coloring principle obtained from cochineal. Carmine occurs in irregular, angular, bright red fragments or as a powder, without odor or taste. When burned it emits an odor resembling that of burned feathers. Carmine is slightly soluble in ammonia water or alkaline liquids, forming a dark purplish red solution. It should not contain more than 25 per cent of water and not more than 12 per cent of ash and should be free from tin, lead, and soluble and insoluble barium compounds. Consult the National Formulary for methods of testing.

USES.—Carmine is a coloring agent.

ALLIED INSECTS AND PRODUCTS.—**Kermes** is a dye produced from *Coccus ilicis* inhabiting *Quercus coccifera*, a native of Greece.

Lac or Shellac is a resinous secretion produced on the bodies of *Lakshadia indica* or other species of *Lakshadia*. Shellac is produced in Burma and India, the insects being cultivated on various plants. The insects resemble cochineal in structure and life history. The secretory glands secrete wax in such quantities that it completely covers the insects and the twigs. Such twigs broken off constitute **stick lac**; a purified form from which the dye has been exhausted is known as **seed lac** and a melted form which is poured on plates is known as **flake lac,** or **shellac,** the latter being the most commonly occurring form in commerce. Shellac contains about 85 per cent of resin. Shellac is used in varnishes, polishes, sealing wax, etc.

ORDER COLEOPTERA, FAMILY MELOIDÆ

This order includes insects having four wings, the posterior pair being membranous and sheathed by the hardened anterior pair. These hardened anterior wings are called elytra, and when folded together nearly cover the body. The mouth parts (mandibles and maxillæ) are well developed. Metamorphosis is indirect. To this order belong the firefly and the various kinds of beetles.

The *Meloidæ* possesses five tarsal joints on each of the front and middle legs. The hind pair have four joints and claws. The integument is rather soft.

CANTHARIDES

Cantharides, Spanish Flies, Russian Flies or Blistering Flies (U. S. P. 1820 to 1942; N. F. 1942 to date) consists of the dried insect, *Cantharis vesicatoria* (Linné) De Geer. *Cantharis* is a Greek word meaning a beetle, *vesicatoria* is from the Latin *vesica*, a bladder, in allusion to the blistering qualities. This insect is found upon certain shrubs of the *Caprifoliaceæ* and *Oleaceæ*, growing in southern and central Europe. The mature insects usually make their appearance in June or July. In the early morning, when the insects are still sluggish from the cold night air, the shrubs are shaken or beaten with poles and the insects collected upon cloths spread on the ground. The insects are killed by plunging them into dilute vinegar, or exposing them to the fumes of hot vinegar, ammonia, sulfur dioxide or by means of chloroform, ether or similar drugs. After this they are carefully dried at a temperature not higher than 40° C. Keep the drug in tight containers and add a few drops of chloroform or of carbon tetrachloride occasionally to preserve the drug from attack by other insects. The commercial supplies are obtained chiefly from southern Russia, Hungary and Spain and to some extent from Roumania, Poland and Sicily.

Spanish fly apparently came hand in hand with medical cruelty and was an heirloom of ancient heroic medication. Hippocrates describes its use in dropsy as early as 375 B.C.

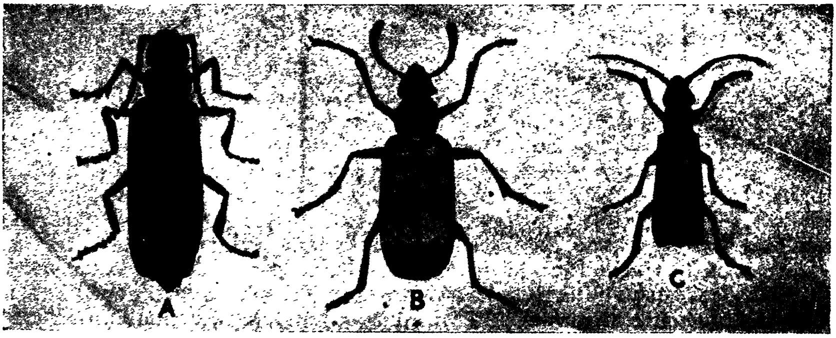


FIG. 366.—*A*, *Cantharis vesicatoria; B*, *Mylabris cichorii; C*, *Cantharis vittata.* (After Snyder.)

DESCRIPTION.—(Fig. 366 *A*.) Oblong, somewhat flattened, from 1.5 to 2.5 cm. in length and 4 to 8 mm. in breadth and of a brilliant green or bluish green metallic luster, being somewhat golden green underneath; head triangular, about 3 mm. in length, separated into 2 lateral lobes by a longitudinal ridge or furrow; antennæ from 4 to 6 mm. in length, consisting of 11 uniseriate joints, the upper being somewhat spheroidal and of a black color; mandibles stout and partly concealed; eyes comparatively small; neck distinct; prothorax angulate, 4-sided; body covered with fine scattered hairs and having 6 long, hairy, black legs, the first and second pair having 5 tarsal joints, the hind pair being 4-parted and having 2 claws at the summit; elytra elongated, nearly equal, almost completely covering the wings, upper portion finely wrinkled, having a brilliant green metallic luster and possessing 2 parallel lines; under surface brown; wings 2, membranous, transparent, light brown and longer and broader than the elytra; odor distinct, penetrating and disagreeable; taste at first slight, afterwards pungent and very acrid.

Powder.—Grayish brown, with shining green particles (see Fig. 367).

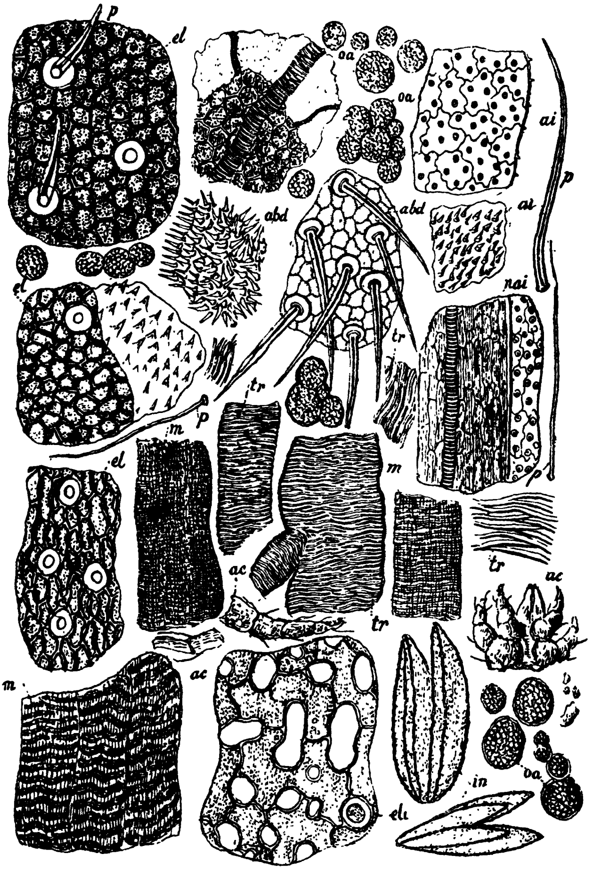


Fig. 367.—Powdered Cantharides: fragments representing the abdomen (*abd*), the membranous wings (*ai*), the mites (*ac*), the elytra showing external surface (*el*) and internal surface (*eli*), and muscles (*m*); *oa* represents the eggs of mites and *p* the long, pointed, 1-celled hairs up to 500 microns long and 20 microns in width at the base; they are from the abdomen, thorax and wings. (After Collin.)

Constituents.—The vesicating principle, cantharidin, 0.4 to 0.8 per cent, the lactone or anhydride of cantharidic acid, occurs in colorless prisms, without odor and taste, nearly insoluble in water, cold alcohol, carbon disulfide and benzol, but soluble in hot alcohol, chloroform, waxes and fixed and volatile oils. In addition, about 12 per cent of a fixed oil, consisting of the glycerides of stearic, palmitic and oleic acid; a resin; and formic, acetic, and uric acids are found. The yield of ash is from 5 to 8 per cent.

STANDARDS.—Cantharides yields not less than 0.6 per cent of cantharidin and not more than 10 per cent of moisture.

USES AND DOSE.—Cantharides is an irritant, a vesicant, and rubefacient. It probably should never be taken internally, as it has the same irritant and vesicant action upon the mucous membrane and comparatively small quantities tend to produce nephritis. Internally it has been given as a diuretic, also as an aphrodisiac.

ALLIED DRUGS.—**Mylabris or Chinese Blistering-flies,** are obtained from *Mylabris cichorii,* indigenous to the East Indies and China. They are elongated, oval or cylindrical (Fig. 366), from 1.8 to 2.5 cm. in length and from 4 to 11 mm. in breadth; elytra or wing-sheaths black, with 2 broad brownish yellow, occasionally golden yellow bands and at the anterior portion a pair of nearly circular brownish yellow spots; heads somewhat triangular and of a jet-black color; mandibles stout and large, partly concealed; antennæ clavate, 11-jointed; eyes large and compound; prothorax wedge-shaped, black; the femora of first and second pairs of legs are covered with yellowish hairs, while the third pair are nearly glabrous and black; odor and taste resembling cantharides.

The powder of mylabris is dark brown and contains numerous, slender, sharp-pointed, blackish hairs, from 200 to 600 microns in length and about 30 microns in width at the base.

Cantharis Vittata (U. S. P. 1820 to 1863), known as the **American Blistering Beetle or Potato Fly,** has pronounced vesicating properties. It is smaller than *C. vesicatoria* and the elytra are black, having a median and marginal yellow stripe.

ORDER HYMENOPTERA, FAMILY APIDÆ

This order includes insects of the highest structural development and instinctive faculties. They have four membranous wings, the anterior pair being the larger. The mouth parts are adapted for both sucking and chewing. Metamorphosis is complete. To this order belong bees, gall-flies, wasps and ants.

The *Apidæ* is a large family characterized by possessing short, stout mouth parts. The posterior tibiæ are devoid of apical spurs. The bees belong to this family

HONEY

Honey, Mel, Clarified Honey or Strained Honey (U. S. P. 1920 to 1947, N. F. 1947 to date) is a saccharine secretion deposited in the honeycomb by the bee, *Apis mellifera* Linné. The generic name *Apis* is Latin for bee, and *mellifera* is from two Latin words meaning to bear honey. Honey bees live in swarms consisting of from 10,000 to 50,000 individuals. The swarms are usually gathered into hives, the bees being thus cultivated for both honey and wax. The individuals may be divided into three classes depending upon differentiation in form and function; thus a hive contains (1) a single queen bee, the fertile female, (2) the males or drones, and (3) the undeveloped females or neuters, which are the working bees. The worker possesses a long, hollow tube formed from the maxillæ and labium, which they insert into the nectaries of the flowers. The nectar, consisting largely of sucrose, is thus drawn up and finds its way through the œsophagus into the honey-sac, where through the action of salivary enzymes it is converted into invert sugar. Upon arrival at the hive the worker deposits the contents of the honey-sac into a special cell of the comb. The beginning of bee-culture is lost in antiquity. The ancient Egyptians placed their hives on rafts, floating them up and down the Nile in accordance with the locality having the most flowers in bloom. Today honey is produced in almost all temperate and tropical countries. Bee farming is an important industry in the United States and Canada. The honey is separated from the wax cells of the honeycomb by expression and straining or by centrifuging.

DESCRIPTION.—A thick, syrupy liquid of a light yellowish or yellowish brown color. It is translucent when fresh but often becomes opaque and granular due to the crystallization of dextrose. It has a characteristic odor and a sweet, faintly acrid taste, the odor and taste varying somewhat depending upon the floral source of the product. Microscopically honey exhibits pollen grains by means of which its floral source may often be established.

CONSTITUENTS.—Principally invert sugar, 50 to 90 per cent, and water. Honey also contains from 0.1 to 10 per cent of sucrose, and small quantities of dextrin, volatile oil and formic acid.

STANDARDS AND TESTS.—Honey must be free from foreign substances such as parts of insects, leaves, etc., but may contain pollen grains. Its specific gravity should be not less than 1.099 at 25° C., it should yield not more than 0.3 per cent of ash and it should be free from starch, dextrin, foreign coloring matter, azo dyes, artificial honey or added invert sugar. Consult the National Formulary for tests and methods. Dextrose and levulose may be demonstrated in honey by the formation of their respective phenylosazones.

USES.—Honey is a nutrient and a demulcent. It is also used as a vehicle similar to syrup, although it possesses more of a laxative action than syrup. Pharmaceutically it finds some use as a pill excipient.

ADULTERANTS.—The most common adulterants of honey are artificial invert sugar, sucrose and commercial liquid glucose.

Yellow Wax or Beeswax (U. S. P. 1820 to date) is the purified honeycomb of the bee, *Apis mellifera* Linné. Wax is secreted in cells on the ventral surface of the last four segments of the abdomen of the worker bees. The wax excretes through pores in the chitinous plates and is employed by the young worker bees in the construction of the comb.

The honeycomb after separation from the honey is melted in water, then cooled and remelted, and finally strained and allowed to harden in molds.

DESCRIPTION.—Beeswax is a solid varying in color from yellow to grayish brown. It has an agreeable honey-like odor, and a faint characteristic taste. When cold it is somewhat brittle and exhibits a dull, granular, non-crystalline fracture. Consult the U. S. Pharmacopœia for characters and tests.

CONSTITUENTS.—Myricin, about 80 per cent, which consists chiefly of myricyl palmitate; myricyl stearate; cerotic acid, about 15 per cent, and cerolein.

USES.—Yellow wax is used as a base for plasters, cerates and ointments. It is also used in polishes.

ADULTERANTS.—Fats, fatty acids, Japan wax, rosin, soap and carnauba wax. (Consult the U. S. Pharmacopœia for methods of detection.)

White Wax or Bleached Beeswax (U. S. P. 1820 to date) is bleached yellow wax. This is accomplished by allowing the melted wax to flow slowly over revolving wetted cylinders, upon which it hardens in thin ribbon-like layers. These are removed and exposed to sunlight and air until bleached, the process usually being repeated, the bleached wax finally being melted and cast into cakes of various shapes. Consult the U. S. Pharmacopœia for characters and tests.

USES.—White wax is employed pharmaceutically in simple cerate and in cold creams.

VERTEBRATA.—See discussion on page 652.

CLASS PISCES, FAMILY GADIDÆ

This, the first class of the vertebrates, includes those oviparous animals which are adapted to life in the water. The majority of fishes have a bony internal skeleton and a scaly protective exo-skeleton. They have a complete cranium and respiration takes place by means of gills. There are two orders: (1) the *Teleostei* or bony fishes and (2) the *Dipnoi* or lung fishes.

The *Gadidæ,* order *Teleostei,* include a number of valuable food fishes such as haddock, codfish, etc.

COD LIVER OIL

Cod Liver Oil (U. S. P. 1851 to date) is the partially destearinated fixed oil obtained from the fresh livers of *Gadus morrhua* Linné and other species of the Family *Gadidæ.* The generic name *Gadus* is from *gados,* the Greek name of the codfish, and *morrhua* is the Latin name of the codfish. Codfish inhabit the North Atlantic Ocean, coming to its shores to spawn in the late winter and spring.

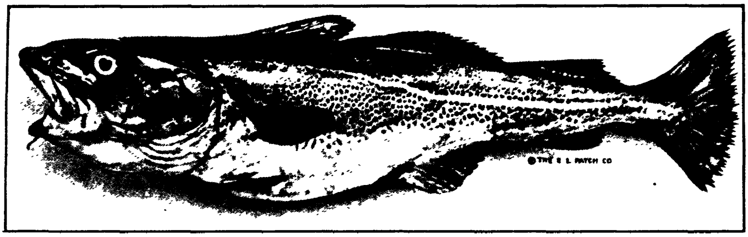


FIG. 368.—The Cod, *Gadus morrhua.* (Courtesy of the E. L. Patch Co.)

The principal fishing grounds are from New England north to Nova Scotia and Newfoundland and along the coast of Norway. Fishing is carried out by trap nets, hand-lines or set-lines. In the early days the fish were cleaned on ship-board, the edible portion being salted and the separated livers thrown into barrels, where through a process of "rotting," the tissue disintegrated and the oil rose to the top. Today, for the production of medicinal oil, the fish are brought to the fish-houses within a few hours after being caught, the livers are removed with care and the gall-bladder is completely separated. The livers are steamed in closed kettles and the oil rises to the top, where it is collected. The air above the oil is replaced by carbon dioxide to prevent oxidation. The oil is strained, filled into tin-lined containers and chilled to a temperature below —5° C. During this chilling process the stearin separates out as a solid and the lighter oil is decanted and filtered. Finally the oil is adjusted to a definite vitamin content by admixture, if necessary of different lots of the oil having higher and lower vitamin values. The liver-marc is often resteamed and pressed for a further yield of oil which is used for technical purposes.

Cod liver oil was exported from Norway as early as the Middle Ages. Its use, however, was for technical purposes only. It was introduced into medicine during the middle of the eighteenth century.

DESCRIPTION.—Cod liver oil is a thin, oily liquid, having a peculiar slightly fishy, but not rancid odor and a fishy taste. It is slightly soluble in alcohol, but freely soluble in ether, chloroform, carbon disulfide and ethyl acetate.

CONSTITUENTS.—The medicinal constituents of cod liver oil are vitamin A (the growth-promoting and antiophthalmic vitamin) and vitamin D (the antirachitic vitamin). The oil consists of glyceryl esters of unsaturated (about 85 per cent) and saturated (about 15 per cent) fatty acids. The unsaturated acids include oleic, linoleic, gadoleic and palmitoleic and the saturated acids include myristic, palmitic and traces of stearic. (Bile salts, and the alkaloids morrhuine and aselline should be absent.) The presence of the former indicates contamination of the livers with gall-bladders and the presence of the latter indicates decomposition.

STANDARDS AND TESTS.—Cod liver oil contains in each gram at least 850 U. S. P. units of vitamin A and at least 85 U. S. P. units of vitamin D.

The vitamin A content of cod liver oil is determined by the amount necessary to cure induced vitamin A starvation in young albino rats of a constant source. The vitamin D potency is determined by the degree of restoration on the proximal end of the tibia or distal end of the radius or ulna of albino rats under the influence of controlled vitamin D starvation. This is known as the "line test." For further standards and the assay processes see the U. S. Pharmacopœia.

Cod liver oil may be flavored by the addition of not more than 1 per cent of any one or any mixture of flavoring substances recognized in the U. S. Pharmacopœia.

STORAGE.—Cod liver oil should be preserved in a cool place, in well-closed containers which have been thoroughly dried before filling. Cod liver oil may be bottled or packaged in a vacuum or in the presence of an inert gas.

USES AND DOSE.—Cod liver oil is used principally for the cure and prevention of rickets, the vitamin D having to do with the utilization of calcium in the formation of the bones and the teeth. Because of the presence of vitamin A, cod liver oil is valuable as a "flesh builder" in wasting diseases and a "growth promoter" in children. Average dose: infants, 4 cc.; adults, 8 cc.

Non-destearinated Cod Liver Oil (U. S. P. 1936 to date) is the crude cod liver oil that has not been chilled so as to separate the stearin. It is permitted to contain not more than 0.5 per cent by volume of water and liver tissue, and it deposits stearin upon chilling, but in all other respects responds to the standards prescribed in the U. S. Pharmacopœia.

HALIBUT LIVER OIL

Halibut Liver Oil (U. S. P. 1942 to date) is the fixed oil obtained from the fresh or suitably preserved livers of the halibut, *Hippoglossus hyppoglossus* L. The name halibut is from *hali* meaning holy and *butte* meaning flounder and refers to a flounder eaten on holy days. The term *hippoglossus* is from the Greek *hippos* meaning horse and *glossus* meaning tongue, and refers to the flat shape of the fish. The halibut inhabits the oceans of the northern hemispheres where commercial fishing is carried on by hand—or set-lines. The livers are processed much the same as cod fish livers.

Description.—See the U. S. Pharmacopœia.

Constituents.—The principal constituents of Halibut Liver Oil are vitamins A and D. Olein, palmitin and cholesterin make up the body of the oil.

Standards and Tests.—Halibut Liver Oil contains in each gram not less than 60,000 U. S. P. units of vitamin A and not less than 600 U. S. P. units of vitamin D. For further standards and tests see the U. S. Pharmacopœia.

Uses and Dose.—Halibut Liver Oil is used for the same purposes as cod liver oil. Its high vitamin potency permits it to be administered in much smaller doses. Gelatin capsules comprise the usual dosage form. The dose is 0.1 gm. as a prophylactic in both infants and adults.

Allied Drugs.—**Burbot Liver Oil** (NNR) is extracted from the livers of the burbot *Lota maculosa* (Fam. *Gadidæ*), a fresh water fish allied to the cod. Burbot Liver Oil has a potency of not less than 4480 U. S. P. units of vitamin A and not less than 640 U. S. P. units of vitamin D, per gram.

Shark Liver Oil (NNR) is extracted from the livers of the shark, principally from the lemon shark *Hypoprion brevirostris*, although any of the following varieties of shark may be the source of the oil: sand shark, *Odontaspis littocalis;* mackerel shark, *Isurus punctatus;* leopard shark, *Triakis semifasciatum;* hammerhead shark, *Sphyrna zygæna;* dusky shark, *Carcharias obscurus;* nurse shark, *Ginglymostoma cirratum;* white shark, *Carcharias milberti,* and the black tip shark, *Carcharias limbatus.* Shark Liver Oil has a potency of not less than 16,500 U. S. P. units of vitamin A, and not less than 40 U. S. P. units of vitamin D, per gram.

Percomorph Liver Oil (NNR) is a mixture of the fixed oils obtained from the fresh livers of the percomorph fishes. The term percomorph is from the Latin *perca* meaning perch and *morph* meaning form, thus a perch-like form. The *Percomorphi* comprise an extensive order of fishes including the perches, basses, mackerels, tunnies, albacores, sword fishes, bonitos, sardines, snappers, groupers and weakfishes; in fact the order includes the majority of the spiny-finned fishes. The oil is obtained from the fresh livers in much the same way as cod liver oil. The following fishes form the principal source of the oil: *Xiphias gladius, Pneumatophorus diego, Thunnus thynnus,* and *Stereolepis gigas,* although several other percomorph are sometimes used. Percomorph Liver Oil contains not more than 50 per cent of other fish liver oil and has a potency of not less than 60,000 U. S. P. units of vitamin A and not less than 8500 U. S. P. units of vitamin D per gram.

Several additional official and unofficial vitamin-containing drugs and preparations will be found in the section on vitamins (see below).

THE VITAMINS

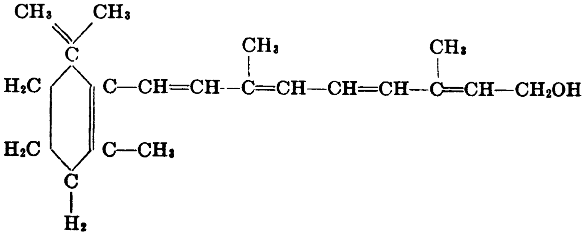
Vitamins are organic compounds required for normal growth and maintenance of life of animals, including man. They do not furnish energy and are not utilized as building units for the structure of the organism, but they are essential for the regulation of the metabolic processes. They act in the form of enzymes during the metabolism of the energy-yielding food constituents.

This definition of vitamins is not without criticism. The substances which we know as vitamins exert no vitamin activity as such, but are active only after chemical transformation into other compounds. Substances as thiamine, riboflavin and niacin are constituents of enzymes. In some cases the same "vitamin" may be part of different enzymes, each having a different catalytic activity. The term "vitamin" as defined above has served a useful purpose and it would be more reasonable to adopt a special terminology for the enzymes containing these vitamins, than to change the present-day definition which in general has been adopted.

VITAMIN A

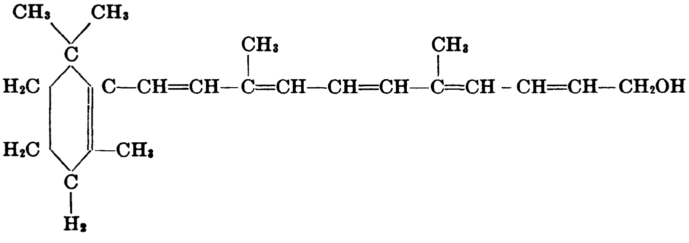
Vitamin A the anti-xerophthalmic vitamin, occurs in three or more forms, namely: Vitamin A_1 or Gadol, from cod liver oil and the liver oils of certain other salt water fish; Galol, a possible geometric isomer of vitamin A_1, from shark liver oil; Vitamin A_2 from fresh water fish oils.

Vitamin A_1 and its isomer have the formula:



Gadol occurs as yellow crystals, having a melting point of 62° to 64° C., and an absorption maximum at 328 millimicrons. Galol occurs as pale yellow needles, having a melting point of 59° to 60° C., and an absorption maximum at 325 millimicrons.

Vitamin A_2 has the formula:



and an absorption maximum at 345 to 350 millimicrons.

The three vitamin A forms are found in the unsaponifiable fraction of the fish oils; are resistant to heat in the absence of air, acids and alkalis; are destroyed by oxidation at all temperatures; and are unstable to light. They may occur as free alcohols or in the ester form.

A group of Provitamin A substances or Carotenoids, including alpha-, beta-, and gamma-carotene, and cryptoxanthine, all of plant origin, are converted in the liver to vitamin A. These compounds are dark red crystals, insoluble in water, acids or alkalis, and very sensitive to oxidation. In the biological assay of vitamin A, 0.6 microgram of pure beta-carotene used to be equivalent to one U. S. P. unit. Vitamin A (but not carotene) may be determined by the Carr-Price method, which is based on the blue color obtained with antimony trichloride. Carotene is measured by colorimetric comparison after chromatographic purification.

The following biological functions of vitamin A may be listed:

1. It is specific in the prevention and cure of xerophthalmia and nyctalopia.
2. Hyperkeratosis of the skin of certain types occurs when vitamin A deficiency is severe.

3. It is useful in overcoming retardation of growth and development when this is due to vitamin A deficiency.
4. It is of value for increasing resistance of the body to infection only when there has been an exhaustion of body reserves and an inadequate ingestion of vitamin A.

DAILY REQUIREMENTS.—Adults 4000 to 5000 units; pregnant and lactating mothers 6000 to 8000 units; children 3000 to 5000 units; infants 1500 units.

SOURCES OF VITAMIN A.—Fish liver oils, liver, egg yolk, cream, cheese, butter, milk; of Carotene: green leafy vegetables, apricots, carrots, sweet potato; of Cryptoxanthin: yellow corn, egg yolk.

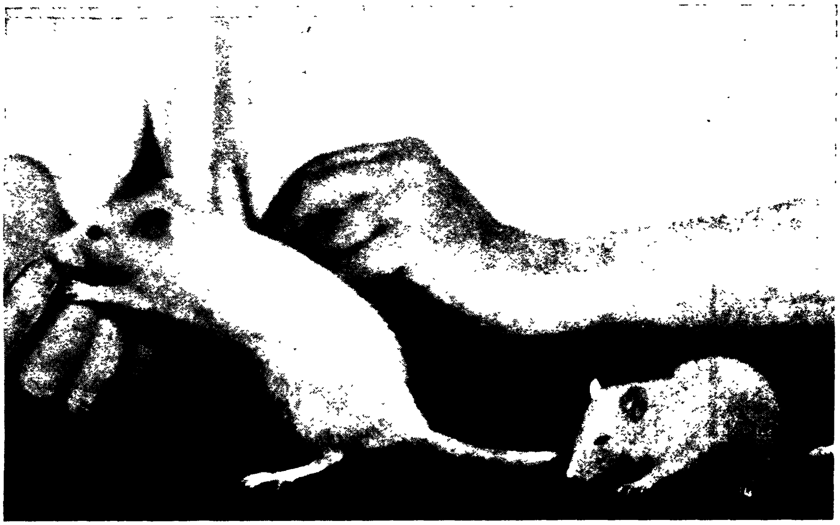
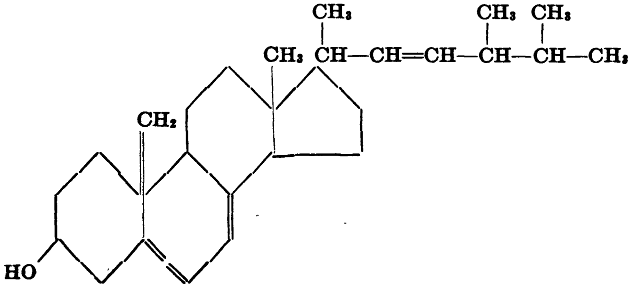


FIG. 369.—Two rats of equal weight were placed on a vitamin A starvation diet: one was fed cod liver oil, the other received none. (Photo, courtesy of Parke, Davis & Co.)

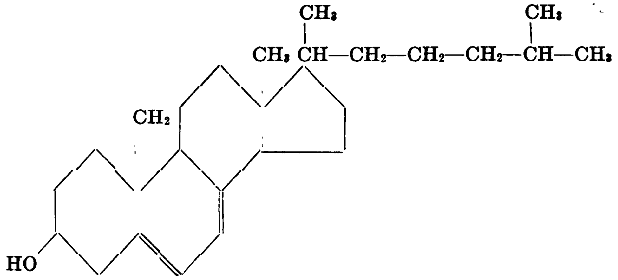
VITAMIN D

The antirachitic vitamin occurs in a number of forms. Four crystalline D vitamers have been isolated and at least 10 provitamins-D are known. They are either ergosterol (vitamin D_2) or cholesterol (vitamin D_3) derivatives. For humans most of the vitamin D activity is supplied from animal sources or from sunshine.

Vitamin D_2, Calciferol, Activated Ergosterol or Viosterol is formed by exposing ergosterol to ultra-violet irradiation or other energy. It is:



Vitamin D_3 is the natural vitamin D found in fish oils and formed in the skin of man and animals following exposure to sunlight. It may be formed by the irradiation of 7-dehydrocholesterol and has the following formula:



These vitamers are white crystalline substances, soluble in fats and organic solvents, and stable to heat and aëration. They exhibit characteristic absorption spectra with a maximum of 205 millimicrons. Vitamin D_2 melts at 115° to 117° C. and vitamin D_3 at 82° to 84° C.

The ultra-violet irradiation of ergosterol, a sterol of vegetable origin found principally in yeast and ergot, produces a series of chemical reactions yielding the following products: Ergosterol → Lumisterol → Tachysterol → Calciferol → Toxisterol → Suprasterols 1 and 2.

In the production of calciferol (viosterol, vitamin D_2) it is important that the conditions of irradiation are such that calciferol is produced to the exclusion of the toxic "over-irradiation" products such as toxisterol. In the early days certain of the irradiated ergosterol products were contaminated with toxisterol because of the failure to give proper consideration to the degree of irradiation. Products such as Ertron synthesized from vegetable sterols by electric energy are said to be free from the toxic sterols.

Drugs and foods are assayed for vitamin D by the rat curative line test. A color reaction with antimony trichloride and ultra-violet absorption are used for certain high-potency products, but in general are not applicable to food products.

Biological Functions.—Vitamin D aids in the utilization of calcium and phosphorus. It is essential to the development and maintenance of strong teeth and bones. Rickets in children and osteomalacia in adults are remedied and prevented by an adequate vitamin D intake. Vitamin D requirements are increased during pregnancy and lactation. One U. S. P. unit is equivalent to 0.025 microgram of crystalline vitamin D_2 (calciferol).

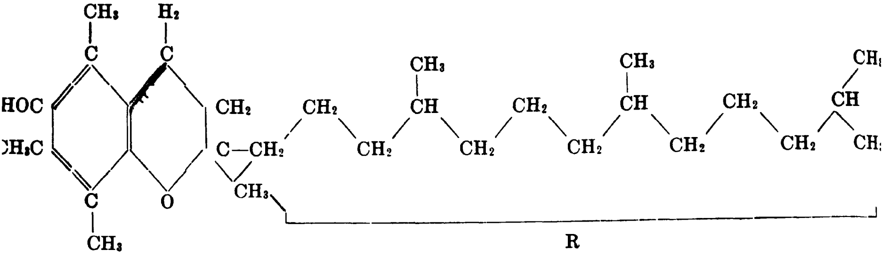
Daily Requirements.—Infants, 400 to 800 units; children, 400 units; pregnant and lactating women, 400 to 800 units; adults: for persons who have no opportunity for exposure to clear sunshine and for elderly persons, the ingestion of small amounts of vitamin D may be desirable. Other adults have little need for vitamin D in the diet. Vitamin D, in excessively large doses over prolonged periods of time, is said to be toxic.

Sources.—Cod liver oil and other fish liver oils; butter, cream and liver; milk and cereals fortified with vitamin D; the activating action of sunlight or ultra-violet light on the skin.

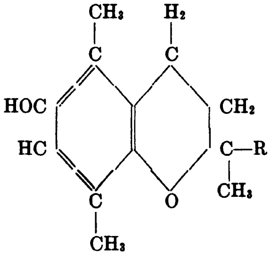
VITAMIN E

Vitamin E designates a group of substances having similar biologic functions. These are alpha-, beta- and gamma-tocopherol of which alpha-tocopherol is the most potent.

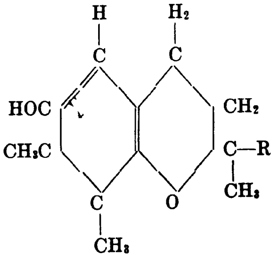
The structural formulæ are as follows:



Alpha-tocopherol



Beta-tocopherol



Gamma-tocopherol

All three vitamers are odorless oils, insoluble in water, but soluble in alcohol, ether and other fat solvents. They are stable to heat in the absence of oxygen, stable to strong acids and visible light, but unstable to ultra-violet light, alkalis and oxidation. The tocopherols are antioxidants, but they are destroyed by rancid fats. The esters of the tocopherols are more stable than the free alcohols. Tocopherols are used to stabilize vitamin A preparations.

One International Unit is equivalent to 1 mg. of pure tocopherol acetate. In the biological assays the average amount of vitamin E is measured which will prevent resorption of the fetus in the female rat. Chemical assays are based on the ability of the vitamers to reduce ferric iron to ferrous iron, and measuring this reduction. Potentiometric titrations can also be used.

Vitamin E is essential for the normal course of pregnancy in rats and also for normal growth and the prevention of paralysis in rats. Its significance in human nutrition has not been established. Some authorities state that for the proper utilization of vitamin A, the tocopherols have to be present in the diet. Others believe that the daily requirement for vitamin A is directly dependent on the vitamin E content of the diet. As far as the use of vitamin E in neuromuscular disturbances is concerned, the many claims and counterclaims are at such variance as to make a critical analysis impossible.

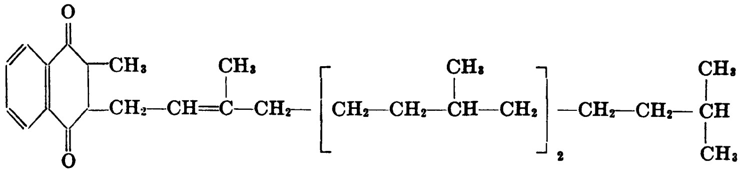
DOSAGE.—No definite dosage has been established, because its clinical use is largely empirical. Daily doses of 15 to 30 mg. of vitamin E given orally have been used in the treatment of habitual abortion.

SOURCES.—Wheat germ oil, cottonseed oil, green leafy vegetables, egg yolk and meat.

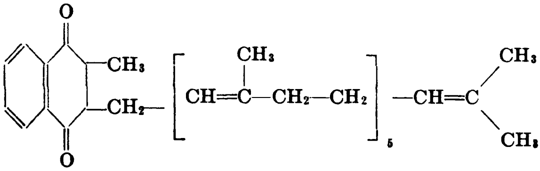
VITAMIN K

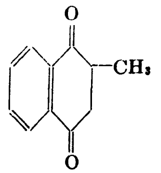
Vitamin K, the coagulation vitamin, occurs naturally in two forms, vitamin K_1 and vitamin K_2. Many synthetic compounds of related chemical constitution also have vitamin K activity.

Vitamin K_1 has the following structure:



Vitamin K_2 has the following structure:





Menadione

Vitamin K_1 is a yellow oil, isolated from alfalfa; vitamin K_2 is a yellow crystalline solid, obtained from purified fish meal.

Menadione, 2-methyl 1, 4-naphthoquinone, is one of the synthetic vitamers, a yellow crystalline powder, apparently with the same vitamin activity as either vitamin K_1 or K_2. Menadione, similar to the natural products, is odorless, soluble in oil and unstable to light and alkalis. Menadione Sodium Bisulfite (U. S. P.) is water-soluble, rather stable to light and is used for injection.

The potency is generally expressed in terms of pure synthetic menadione. Oxidation and reduction methods as well as colorimetric methods have been established. A biological method for the estimation of vitamin K is based upon its physiological function.

Vitamin K is said to be necessary for the formation of prothrombin in the liver. Since prothrombin is a constituent of the blood essential for normal clotting, vitamin K therefore plays an indirect rôle in that process. A deficiency of prothrombin (hypoprothrombinemia) results in a prolongation of the clotting time.

Deficiency of vitamin K is seldom due to dietary origin. Since vitamin K is formed by microörganisms in the intestines, it seems reasonable to conclude that normal humans are largely independent of a dietary supply. Inadequate absorption does occur in cases of obstruction, jaundice, diarrhea and during the excessive use of laxatives.

The special use of vitamin K lies in its prevention of hemorrhagic disease of the new-born.

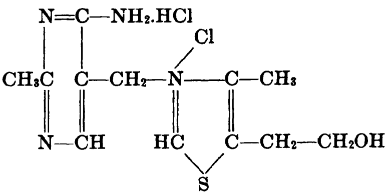
Definite daily requirements have not as yet been determined. The therapeutic dose for the cure or prophylaxis of hypoprothrombinemia is 1 to 2 mg. daily. Toxic effects have been noted in animals following the administration of large doses.

Sources.—In addition to the commercial sources mentioned above vitamin K occurs in green leafy materials such as spinach, kale, etc., in tomatoes and in vegetable oils.

THE VITAMIN B COMPLEX

The **Vitamin B Complex** includes a number of dietary essentials which are found in significant quantities in liver and yeast. Originally it was not recognized that these natural extracts contained more than one vitamin but as research progressed several components were eventually isolated. In an early classification the "B Complex" was subdivided into vitamins B_1 and B_2, the former being thermolabile and the latter thermostable. We now know the structure of at least nine and possibly ten substances recognized as members of this group. The vitamin status of some of them, although included in the group is not as yet clearly established. The members of the group have little in common from a chemical standpoint.

Thiamine Hydrochloride or Vitamin B_1 has the following structural formula:



It is in colorless, monoclinic needles, melting at 248° to 250° C., soluble in water, slightly soluble in alcohol, and insoluble in oil; it is relatively stable in dry form to heat and light; in aqueous solution the pH is about 3.5, and such solutions may be sterilized by heating for twenty minutes at 120° C. or for one hour at 100° C., without appreciable loss of potency. In foods, however, there is some destruction of the vitamin during cooking.

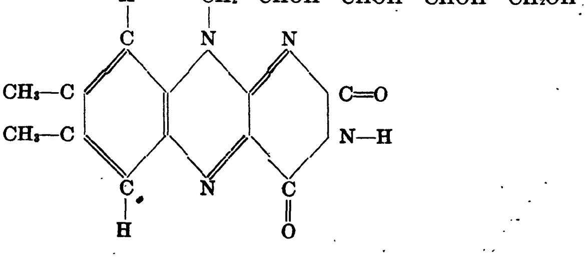
The U. S. P. or International Unit of potency is the equivalent of 3 micrograms of crystalline thiamine hydrochloride. It is assayed chemically by the thiochrome method and microbiologically by the yeast fermentation method. The vitamin occurs in nature in the free form or as thiamine pyrophosphate (cocarboxylase) or as the cocarboxylase protein complex.

Vitamin B_1 plays a fundamental rôle in intermediate carbohydrate metabolism in all living cells and is therefore essential for the normal functioning of all body organs and tissues. In the body thiamine is converted to the pyrophosphate (cocarboxylase) which functions as a coenzyme in the decarboxylation of pyruvic acid to form acetaldehyde and carbon dioxide. The vitamin is not stored in the body to any appreciable extent, the excess being largely eliminated or destroyed. Marked deficiency symptoms which respond to thiamine therapy are emotional hypersensitivity, loss of appetite, susceptibility to fatigue, muscular weakness and beriberi. Symptoms of mild or subacute thiamine deficiency are less clearly defined.

DAILY REQUIREMENT.—Adults, 1.2 to 2 mg.; infants, 0.4 to 0.8 mg.; children, 1 to 1.8 mg. The therapeutic dose is 5 to 50 mg.

SOURCES.—Enriched cereals, whole grain cereals, milk, legumes, meats. Special sources include yeast, liver concentrates and synthetic thiamine.

Riboflavin, Vitamin B_2, Vitamin G, or Lactoflavin has the following structure:



The substance was first identified in milk and because of its yellow color was known as "lactochrome" and later as "lactoflavin." It occurs naturally in the free form or in various chemical complexes with protein, phosphoric acid, adenine or nucleic acid.

Riboflavin is slightly soluble in water and in alcohol, and insoluble in lipoidal solvents. It crystallizes from absolute alcohol as yellow, needle-shaped crystals melting with decomposition at 282° C. It is stable to heat in dry form and in acid solution and rather stable to oxidation, but is unstable in alkaline solution and is very sensitive toward light. In solution it possesses an intense greenish yellow fluorescence. When exposed to light in acid solution the vitamin is changed to lumichrome, while when irradiated in alkaline solution a degradation split occurs yielding a new pigment, lumiflavin. Neither lumichrome nor lumiflavin possesses physiological activity.

One milligram of Riboflavin is equivalent to 400 Sherman-Bourquin units. The vitamin is assayed biologically by the rat-growth method; the microbiological method is official for drugs and is also the tentative method in food analysis, and a third method utilizes the fluorescent properties of the substance.

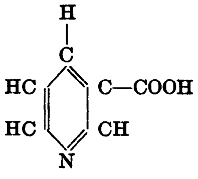
Riboflavin, following its injection, combines with phosphoric acid and protein to form an enzyme called "Warburg's Yellow Enzyme" or "the yellow oxidation enzyme." Apparently riboflavin cannot be synthesized by animal cells and therefore must be supplied in the diet. Riboflavin functions, as the yellow enzyme, in tissue oxidation. Deficiency symptoms are characterized by cheilosis, glossitis and peeling of the skin. Ocular disturbances are characterized by itching, burning and a sensation of roughness of the eyes accompanied by mild photophobia.

Daily Requirement.—Adults, 1.6 to 3 mg.; infants, 0.6 to 1.8 mg.; children, 1.8 to 2 mg. The therapeutic dose is 3 to 15 mg.

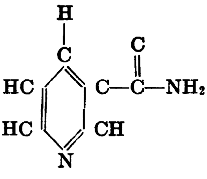
Sources.—Milk, egg yolk, liver, meats, green leafy vegetables and bread.

Niacin or Nicotinic Acid, and Niacinamide or Nicotinamide.—The names Niacin and Niacinamide have been recommended by The Food and Nutrition Board of the National Research Council because these names do not have the phonetic similarity to nicotine as do the older names.

They have the following structural formulas:



Niacin



Niacinamide

These substances have been known since 1867 and their occurrence in animal tissues was recognized in 1912. No dietary importance was attached to them, however, until 1937, when it was reported that liver, a source rich in niacin, cured "black tongue" in dogs, which had long been considered to have a counterpart in the human disease known as pellagra.

Niacin occurs as colorless, odorless needles or as a crystalline powder. It is soluble in water and alcohol but is insoluble in lipoidal solvents. It is quite stable both in dry form and in solution. The amide, also a colorless, crystalline powder, is slightly hygroscopic, and has a slightly bitter taste. It melts at about 122° C. and is more soluble in water and alcohol than the acid. It is quite stable in dry form and in solution. Prolonged exposure to light should be avoided.

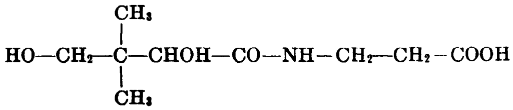
In nature, the vitamin is found as the free acid or its amide, chemically bound in a number of enzyme systems. Niacinamide is the functional group in co-enzymes I and II, diphosphopyridine nucleotide and triphosphopyridine nucleotide respectively. These compounds play an important rôle in tissue respiration, carbohydrate metabolism and in fermentations by transporting hydrogen.

Potencies of niacin are expressed in terms of milligrams rather than in units. The substance is assayed biologically by the black-tongue curative and the chick-growth methods. The microbiological method is official for drugs and foods. A chemical colorimetric method using cyanogen bromide and various amines has also been proposed. While most of the symptoms of pellagra are due to a deficiency of niacin, it is now believed that the various manifestations of the disease are not all due to the deficiency of a single vitamin. The appropriate administration of niacin leads to a disappearance of the alimentary, dermal and other lesions characteristic of the disease, but the vitamin is without influence upon the polyneuritis or cheilosis so frequently observed in pellagrous patients. These latter require the administration of thiamine and riboflavin.

DAILY REQUIREMENT.—Adults, 12 to 20 mg.; infants, 6 to 12 mg.; children, 4 mg. The maximum therapeutic dose of niacin is 500 mg. per day.

SOURCES.—Meats, liver, eggs, milk, cereals and nuts.

Pantothenic Acid is the designation for the factor in the vitamin B complex necessary for the proper growth of rats. It is also known as the "chick antidermatitis factor." The substance has the following formula:



$$\mathrm{HO{-}CH_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}CHOH{-}CO{-}NH{-}CH_2{-}CH_2{-}COOH}$$

It is dextrorotatory and is usually marketed as the calcium salt, **Calcium Pantothenate Dextrorotatory.**

The acid itself is a viscous oily liquid, soluble in water and some organic solvents but insoluble in benzene and chloroform. Pantothenic acid is unstable toward acids, alkalis and prolonged heating when in aqueous solution. The calcium salt is relatively thermostable, but is unstable toward alkalis, acids, ferric salts and calcium precipitants. The salt is a white, crystalline powder.

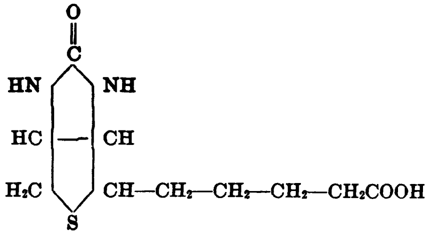
The potency of this vitamin is usually expressed in milligrams of the acid. It is assayed biologically by the chick growth method, and by microbiological methods, employing either *Lactobacillus casei* or *Lactobacillus arabinosus.* To date no chemical test for this substance has been found.

Although pantothenic acid is found in most living tissue its definite rôle is unknown and no definite pantothenic acid deficiency has been demonstrated in man.

DAILY REQUIREMENT.—Unknown. Therapeutic dose, 1 to 100 mg.

SOURCES.—Liver, kidney, yeast, milk, cereals, legumes and nuts.

Biotin or Vitamin H, the yeast growth, or the anti-egg-white injury factor, has the following structural formula:



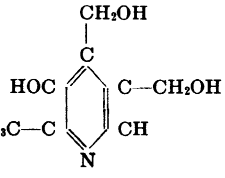
Free biotin is water and alcohol soluble but is relatively insoluble in ether, chloroform and petroleum ether. The substance is heat stable and does not decompose when heated with acids or alkalis. The pure vitamin melts at 230° to 232° C., while its methyl ester melts at 166° to 167° C. Biotin is active in both animals and microörganisms, and the methyl ester is active for animals but not for all microörganisms. Amounts of biotin are expressed in milligrams and microbiological methods have supplanted the rat- or chick-curative method.

Biotin deficiency symptoms have not as yet been definitely established. The vitamin, however, is claimed to be necessary for the maintenance of health. Some of the symptoms due to a deficiency of biotin are said to be seborrheic dermatitis, pallor of the skin, mental depression and muscular pains. Avidin, a raw-egg-white protein induces biotin deficiency by forming a non-absorbable avidin-biotin complex.

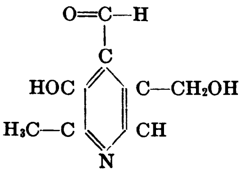
Daily Requirement.—Unknown. Therapeutic dose, parenteral, 0.15 to 0.3 mg. (150 to 300 micrograms) daily.

Sources.—Egg yolk, liver, kidney, yeast, grains and milk.

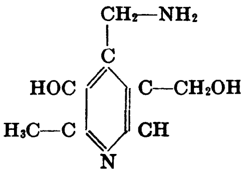
Pyridoxine or Vitamin B_6 consists of a group in which pyridoxine is one of three members. The three forms known at the present time are as follows:



Pyridoxine



Pyridoxal



Pyridoxamine

The three forms are about equally active for rats but not so for microörganisms. Pyridoxine melts at 204° to 205° C. The substance is soluble in water, alcohol and acetone and slightly soluble in other organic solvents. It is stable toward heat, concentrated acid and alkali, but is destroyed by light. Potencies of pyridoxine are expressed in milligrams or micrograms. Biological methods of assay include the rat growth and acrodynia cure test. Microbiological procedures use *Streptococcus Carlsbergensis*, *Lactobacillus casei*, *Streptococcus fæcalis*. Some chemical methods showing promise recently have been published.

Pyridoxine appears to be related to the metabolism of fats and amino acids. Its exact biological function is, however, not fully understood. Rats deprived of pyridoxine develop a symmetrical dermatitis (acrodynia) and fail to grow. Dogs and other animals develop microcytic anemia and exhibit a degeneration of striated and cardiac muscles.

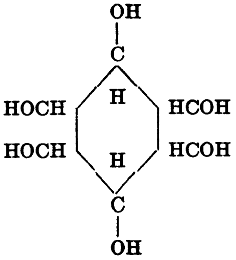
Since no definite vitamin B_6 deficiency syndrome has been recognized in man, no diagnosis based on clinical symptoms is possible. It has been pointed out, however, that pyridoxine deficiency may accompany other deficiencies of the B complex. The failure of patients suffering from B complex deficiency to recover completely when thiamin, riboflavin and nicotinic acid were administered has been noted. Such patients continued to complain of extreme nervousness, irritability, insomnia, abdominal pain and difficulty in walking. Parenteral administration of pyridoxine hydrochloride in such patients is claimed to have produced dramatic relief.

Daily Requirement.—Unknown. Therapeutic dose, 25 to 200 mg., orally or parenterally.

Sources.—Meats, seafoods, cereals, legumes and yeast.

Other Water-soluble Factors Found in Liver and Yeast, Whose Vitamin Status Has Not Been Clearly Established

Inositol, known to chemists for a long time, has the following formula:



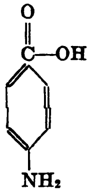
Of the eight possible isomers, only one (i-inositol) is optically inactive. This latter isomer is the only one that is active as a growth factor. It occurs in the free form and in various complexes such as phytin and liposterol. Inositol is soluble in water and insoluble in petroleum ether and in absolute alcohol. It is stable toward heat, strong acids and alkalis. The anhydrous form melts at 225° to 226° C. Amounts of inositol are expressed in milligrams rather than in units. Microbiological methods employing *Sacch. cerevisæ* or *Neurospora sitophilia* have been used in favor of chemical or biological assay procedures.

The nutritional status of inositol is controversial. Under certain conditions it appears to prevent alopecia, to have lipotropic activity and influence gastric motility. Conflicting observations indicate that inositol is not a dietary essential or that the substance may be involved in intestinal flora activity. Because no specific deficiency syndromes in man have been attributed to inositol, its exact rôle in human metabolism is unknown.

Daily Requirement.—Unknown. No therapeutic claims for inositol have been recognized.

Sources.—Cereals, citrus fruits, certain meats, milk and yeast.

Para-aminobenzoic Acid has long been known as a synthetic organic chemical compound, and has the following formula:

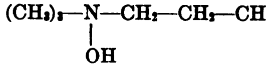


It has only recently been recognized to be a component of the B-Complex. The substance occurs in the free state or in the acetylated or conjugated form. It is soluble in boiling water and alcohol and stable toward acids and alkalis. The colorless crystals melt at 186° to 187° C. It is destroyed by ferric salts and oxidizing agents. Potency is expressed in terms of milligrams of p-aminobenzoic acid. Both chemical and microbiological methods have been proposed for the assay of this compound. Removal of p-aminobenzoic acid from the diet causes achromotrichia in rats and failure of growth in chicks. It is active in neutralizing the anti-bacteriostatic effect of some sulfa drugs. Therapeutic claims for man have not been recognized.

Daily Requirement.—Unknown. Therapeutic claims for man have not been recognized, though a daily dose of 200 mg. is given.

Sources.—Meats and vegetables.

Choline as a component lecithin and a phospholipid has been known for many years. It has the following formula:



$$(CH_3)_3-\underset{\underset{\displaystyle OH}{|}}{N}-CH_2-CH_2-CH$$

Recently some authorities have recognized it as a member of the B-Complex. Choline is marketed as the chloride. Both choline and choline chloride are soluble in water and alcohol, but are insoluble in ether, benzene and petroleum ether. They are stable to heat in acid solution but unstable in alkaline solution. They are extremely hygroscopic. Potencies are expressed in milligrams of choline. Colorimetric as well as microbiological procedures have been used as methods of assay.

Choline affects the fat transport and indirectly carbohydrate metabolism. Deficiency of choline leads to hemorrhagic kidney degeneration. It is one of the factors in the pancreas which prevents development of fatty livers in depancreatized animals. It has been reported that choline may be useful in the treatment of human liver cirrhosis; however, definite therapeutic claims have not been reported.

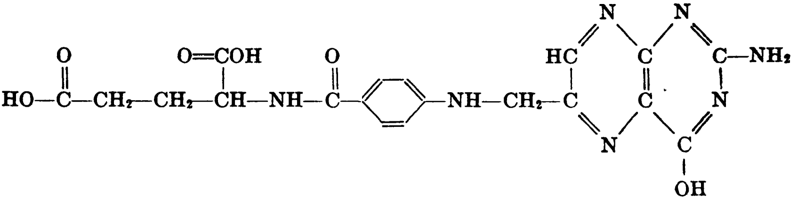
Daily Requirement.—Unknown. Therapeutic dose, undetermined.

Sources.—Egg yolk, heart, liver, sweetbreads, milk, fish, root vegetables, fruits and grains.

Dietary Factors Concerned With Nutritional Anemias

A number of water-soluble acidic materials found in yeast, liver and green leaves have been isolated and shown to have activity in preventing anemia in chicks and other animals, and in promoting growth in chicks and in rats as well as in certain microörganisms such as *Lactobacillus casei*, *Streptococcus lactis*, and *Streptococcus fæcalis*. Various names have been applied to these factors such as **Vitamin B_C, L. casei factor, Vitamin M** or **"folic acid,"** and **pteroglutamic acid.**

The crystalline *L. casei* factor of liver has been synthesized and is reported to have the following structure:



It is a yellow crystalline powder.

It now appears that vitamin B_c and crystalline *L. casei* factor as isolated from liver are identical. A crystalline precursor of vitamin B_c has been isolated from yeast and has tentatively been named vitamin B_c Conjugate. The latter substance can be converted into vitamin B_c by enzymatic treatment.

The term vitamin M refers to a growth and anti-anemia factor for monkeys. Its nature has not been established but it is believed to be vitamin B_c because of its biological properties. The term "folic acid" has been used by different investigators to designate any one of a number of these biologically similar factors. The potency is expressed in micrograms of folic acid. While microbiological methods have been devised for the determination of "folic acid" the anti-anemia potency must be measured by using chicks or rats.

Deficiency of this vitamin causes retardation of growth and macrocytic anemia in the chick and rat. The synthetic material has recently been claimed to be of value in macrocytic anemia, including pernicious anemia in the human.

Daily Requirement.—Unknown.

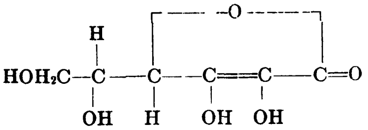
Sources.—Yeast, liver, grass, and green leafy vegetables.

In addition to the known vitamins which have been discussed, there are a number of compounds which at the present time are thought to be vitamins. As far as their importance in human nutrition is concerned we can only speculate and until further investigations are carried out and their value more definitely established, mention of them here is omitted.

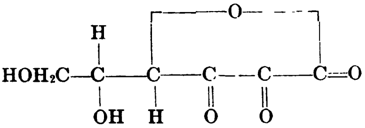
VITAMIN C

Ascorbic Acid or Vitamin C (U. S. P. and N. N. R.) and **Sodium Ascorbate Injection** are the official forms of the antiscorbutic vitamin found naturally in several forms: the reduced form (ascorbic acid), the oxidized form (dehydroascorbic acid) and as ascorbinogen (the protein complex).

The formula for the reduced form is as follows:



while the oxidized form has the following structure:



Ascorbic Acid is an optically-active compound, but only the levo-form is biologically active. It is an odorless, white, crystalline substance which slowly darkens upon exposure to light. It melts at 190° to 192° C., and is soluble in water, alcohol, propylene glycol and glycerin, but is insoluble in ether and benzene. Dry ascorbic acid is fairly stable but aqueous solutions are rapidly decomposed when in contact with air. Ascorbic acid is a relatively strong reducing agent; it is reversibly oxidized to dehydroascorbic acid. The latter can be further oxidized to 2,3,diketo-l-gulonic acid which is inactive. Alkalis accelerate both oxidations but acids retard them. Since ascorbic acid is the least stable of all vitamins special consideration must be given to this factor when planning diets.

The potency is expressed in milligrams of ascorbic acid. Although bioassay methods based on the curative or preventative effect of ascorbic acid continue to be used, they are gradually being displaced by chemical methods using the 2,6, dichlorophenolindophenol acid and in some cases, the 2,4,dinitrophenylhydrazine procedures.

Vitamin C appears to be essential for the proper formation as well as the maintenance of intercellular material in tissues, especially of bones and teeth. It prevents and cures scurvy and is claimed by some authorities to be of value in increasing resistance to infection. It has definitely been established to be of clinical importance in relation to the healing of wounds. Ascorbic acid is an important factor in cellular oxidation and reduction processes.

DAILY REQUIREMENT.—Adults, 30 to 75 mg.; children, 30 to 100 mg.; infants, 30 mg. Average dose, 50 mg.

SOURCES.—Fresh fruits, potatoes, green leafy vegetables and seafoods.

Citrin or Vitamin P are terms used to designate a dietary factor, other than ascorbic acid, necessary to the maintenance of proper capillary resistance. At present vitamin P has not been identified in pure form. Several flavone glycosides including eriodictin and hesperidin have been found to have vitamin P activity.

Tentative methods of assay are based upon measurements of capillary fragility in test animals. Various fruit extracts have been used as standards. Citrin restores permeable and fragile capillaries to their normal state. It appears to be of value in the treatment of conditions of the skin (nutritional purpurea and purpurea of measles) in man. Its rôle as a dietary essential has as yet not been definitely established.

SOURCES.—Hungarian red pepper, citrus fruits and black currants. So far no animal sources have been demonstrated.

VITAMIN PREPARATIONS

VITAMINS A AND D:

Oleovitamin A, Natural Vitamin A in Oil (U. S. P. 1940 to date) is either fish liver oil, or fish liver oil diluted with edible vegetable oil, or a solution of vitamin A concentrate from natural sources (animal) in fish liver oil or edible oil. Oleovitamin A contains in each gm. not less than 50,000 and not more than 65,000 U. S. P. Units of vitamin A, and not more than 1000 U. S. P. Units of vitamin D. Average daily dose 0.1 cc. Preparation: Oleovitamin A Capsules.

Oleovitamin A and D (U. S. P. 1940 to date) is either fish liver oil, or fish liver oil diluted with an edible vegetable oil, or a solution of vitamin A and D concentrates in fish liver oil or in an edible vegetable oil. The vitamin A shall be obtained from natural (animal) sources and the vitamin D may be obtained from natural (animal) sources or may be synthetic Oleovitamin D. Oleovitamin A and D contains in each gram not less than 850 and not more than 1100 U. S. P. Units of vitamin A, and not less than 85 and not more than 110 U. S. P. Units of vitamin D. Average daily dose, 8 cc.

Concentrated Oleovitamin A and D (U. S. P. 1940 to date) is either fish liver oil, or fish liver oil diluted with an edible vegetable oil, or a solution of vitamin A and D concentrates in fish liver oil or in an edible vegetable oil. The vitamin A is obtained from natural (animal) sources and the vitamin D may be from natural (animal) sources or may be synthetic Oleovitamin D. Concentrated Oleovitamin A and D contains in each gram not less than 50,000 and not more than 65,000 U. S. P. Units of vitamin A, and not less than 10,000 and not more than 13,000 U. S. P. Units of vitamin D. Average daily dose, 0.1 cc. Preparation: Concentrated Oleovitamin A and D Capsules.

Synthetic Oleovitamin D, Viosterol in Oil (applying only to Activated Ergosterol in Oil) (U. S. P. 1936 to date) is a solution of activated ergosterol, or activated 7-dehydrocholesterol, in an edible vegetable oil. Synthetic Oleovitamin D contains in each gram not less than 10,000 U. S. P. Units of vitamin D. Average daily prophylactic dose, 0.1 cc.

Cod Liver Oil (U. S. P. 1851 to date) (see page 662) contains not less than 850 U. S. P. Units of vitamin A and not less than 85 U. S. P. Units of vitamin D per gram. Average dose, 8 cc. Preparation: Cod Liver Oil Emulsion.

Non-Destearinated Cod Liver Oil (U. S. P. 1936 to date) (see page 663) has the same requirements as for Cod Liver Oil.

Halibut Liver Oil (U. S. P. 1942 to date) (see page 663) contains in each gram not less than 60,000 U. S. P. Units of vitamin A and not less than 600 U. S. P. Units of vitamin D. Average daily dose, 0.1 cc. Preparation: Halibut Liver Oil Capsules.

Carotene in Oil and Carotene With Vitamin D Concentrate in Oil are non-official preparations in which the carotene and vitamin D are dissolved in cottonseed oil. Both preparations have a vitamin A potency of not less than 7500 U. S. P. Units per gram, and the latter has a vitamin D potency of not less than 1000 U. S. P. Units per gram.

Vitamin D_2 or Drisdol (non-official) is prepared by ultra-violet irradiation of ergosterol and contains not less than 40 U. S. P. Units of vitamin D per microgram.

Burbot Liver Oil (non-official) (see page 664) contains not less than 4480 U. S. P. Units of vitamin A and not less than 640 U. S. P. Units of vitamin D per gram.

Percomorph Liver Oil (non-official) (see page 664) contains not less than 60,000 U. S. P. Units of vitamin A and not less than 8500 U. S. P. Units of vitamin D per gram.

Shark Liver Oil (non-official) (see page 664) contains not less than 16,500 U. S. P. Units of vitamin A and not less than 40 U. S. P. Units of vitamin D per gram.

VITAMIN K:

Menadione, 2-Methyl-Naphthoquinone, Menaphthene or Menaphthone (U. S. P. 1942 to date). Average dose, 1 mg. Preparation: Menadione Tablets.

Menadione Sodium Bisulfite or Menadione Bisulfite (U. S. P. 1947 to date) contains not less than 49 per cent of menadione. Average parenteral dose, 2 mg. Preparation: Menadione Sodium Bisulfite Injection.

VITAMIN B COMPLEX:

Thiamine Hydrochloride, Vitamin B_1, Vitamin B_1 Hydrochloride or Aneurine Hydrochloride (U. S. P. 1940 to date) contains not less than 98 per cent of $C_{12}H_{17}ClN_4OS.HCl$. Average dose, 5 mg. Preparations: Thiamine Hydrochloride Injection, Thiamine Hydrochloride Tablets.

Rice Polishings, Rice Bran, Tikitiki (U. S. P. 1942 to date) consists of the fine flaky pericarp and spermoderm fragments, the embryo, aleurone layer, and outer adhering cells of the starchy endosperm of the grain of *Oryza sativa* Linné.

Rice Polishings Extract (U. S. P. 1942 to date) contains in each cubic centimeter not less than 20 U. S. P. Units of vitamin B_1, and represents approximately 14.5 gm. of rice polishings. Average dose, 8 cc.

Riboflavin, Lactoflavin, Vitamin B_2 or Vitamin G (U. S. P. 1942 to date), when dried at 100° for three hours, contains not less than 98 per cent of $C_{17}H_{20}N_4O_6$. Average dose, 5 mg. Preparations: Riboflavin Injection and Riboflavin Tablets.

Nicotinic Acid or Niacin (U. S. P. 1940 to date), when dried over sulfuric acid for three hours, contains not less than 99.5 per cent of $C_6H_5O_2N$. Average dose, 25 mg. Preparations: Nicotinic Acid Tablets.

Nicotinamide, Nicotinic Acid Amide or Niacinamide (U. S. P. 1942 to date) when dried over sulfuric acid for four hours, contains not less than 98.5 per cent of $C_6H_6N_2O$. Average dose, 25 mg. Preparations: Nicotinamide Injection, Nicotinamide Tablets.

Pyridoxine or Vitamin D_6 (non-official). Average dose, 5 mg.

Dried Yeast or Dry Yeast (U. S. P. 1944 to date) consists of the dried cells of any suitable strain of *Saccharomyces cerevisiæ* Meyen. Dried Yeast contains not less than 40 per cent of protein and, in each gram, the equivalent of not less than 0.12 mg. of thiamine hydrochloride, 0.04 mg. of riboflavin, and 0.25 mg. of nicotinic acid. Average dose, to be determined by the physician. Preparation: Dried Yeast Tablets.

Triasyn B Capsules and Triasyn Tablets (U. S. P. 1947 to date) contain in each capsule or tablet not less than 2 mg. of thiamine hydrochloride, 3 mg. of riboflavin, and 20 mg. of nicotinamide.

Hexavitamin Capsules and Tablets (U. S. P. 1947 to date) contain not less than 5000 U. S. P. Units of vitamin A from natural (animal) sources, 400 U. S. P. Units of vitamin D from natural (animal) sources or as activated ergosterol or activated 7-dehydrocholesterol, 75 mg. of ascorbic acid, 2 mg. of thiamin hydrochloride, 3 mg. of riboflavin, and 20 mg. of nicotinamide per capsule or tablet.

VITAMIN C:

Ascorbic Acid or Vitamin C (U. S. P. 1940 to date), when dried in a vacuum desiccator over sulfuric acid for three hours, contains not less than 99 per cent of $C_6H_8O_6$. Average dose, 50 mg. Preparation: Ascorbic Acid Tablets.

Sodium Ascorbate Injection (U. S. P. 1947 to date) is a sterile solution of sodium ascorbate in water for injection. Average dose of ascorbic acid, 0.1 gm.

Manufacturers supply various other vitamins and combinations and dosage forms of the vitamins, such as capsules, tablets, emulsions, mixtures, etc.

OTHER PRODUCTS FROM FISH.—**Ichthyocolla or Isinglass** (U. S. P. 1820 to 1905), which is the swimming-bladder of the Russian sturgeon, *Acipenser huso* and other species. The swimming-bladder or "sound" is removed and scraped to remove the outer layer. The inner layer is dried, usually stretched into sheets on pegs. Its principal constituent is gelatin and it has been used as an emollient and a protective.

American Isinglass consists of the sounds of the hake (*Gadus merluccius*) or the weakfish (*Otolithus regalis*).

CLASS REPTILIA, ORDER OPHIDIA, FAMILY CROTALIDÆ

Reptiles comprise one of six classes of vertebrates, being placed above the amphibians but below the birds. They begin the series of higher vertebrates which never breathe with gills. The class includes five orders comprising turtles, lizards, snakes, crocodiles and alligators. The order *Ophidia* includes the snakes, of which the family of pit vipers (*Crotalidæ*) is of special interest. To this family belong the rattlesnake, the water moccasin and the copperhead, all of which have fangs connected with special poison glands, by means of which a toxin is injected into the circulation of any animal they may bite. To counteract this poison, **North American Antivenin (Nearctic Crotalideæ Antivenin)** has been prepared. (See Antivenins, page 76.)

CLASS AVES, FAMILY PHASIANIDÆ

The *Aves* or birds are warm-blooded, oviparous vertebrates differing from other vertebrates in possessing feathers. The forelegs are modified into wings.

The *Phasianidæ* include chickens, turkeys, partridges, and other fowl-like birds with usually a terrestrial but sometimes a tree habit.

They have short, rounded wings and stout legs terminating in sharp-clawed toes especially adapted to scratching.

Egg, Hen's Egg or Fresh Egg (U. S. P. 1851 to 1882; N. F. 1916 to 1947; in culture media N. F. 1936 to date) is the recently laid egg of *Gallus domesticus* Temminck. *Ovum* is Latin for egg; *Gallus* is the Latin name of the hen, and *domesticus* is Latin, meaning domesticated. Chickens are raised in the United States and practically all other temperate and tropical countries for their flesh and for the production of eggs. Those fowls having Mediterranean ancestry, of which the Leghorns are the best known variety, are particularly valuable as egg producers.

DESCRIPTION.—Hens' eggs are ovoid, up to about 7 cm. in the longer diameter. They consist of an outer whitish or yellowish white calcareous shell enclosing a thin membrane which surrounds a mass of colorless albuminous matter known as the egg white. Embedded in this egg white is a globular, yellowish or reddish yellow egg yolk.

CONSTITUENTS.—The egg shell consists almost entirely of calcium carbonate with small quantities of magnesium and calcium phosphates and organic matter. The shell constitutes about 11 per cent of the weight of the egg.

The white, constituting about 57 per cent of the total weight of the egg, consists of about 85 per cent of water, 12 per cent of protein matter and 2.5 per cent of ovamucoid (a mucin-like substance), with traces of fats and mineral salts.

The egg yolk, comprising about 32 per cent of the total weight of the egg, consists of about 52 per cent water, 20 to 30 per cent of fat, about 16 per cent of a protein known as vitellin, about 1.5 per cent of the protein nuclein, which is rich in phosphorus, about 7 per cent of lecithin, about 0.5 per cent of cholesterin and small quantities of cerebrin (found in brain and nerve tissue) and mineral salts. Vitamins A, B and C are also present in egg yolk. Vitamin B_2 is present in egg-white.

USES.—Egg shell has been used as an antacid. Egg white is a clarifying agent and as such has been employed domestically for a long time in coffee making. It is also employed as an antidote for corrosive poisons where it acts both by combining with the corrosive agent and by protecting the mucous tissues mechanically. Egg yolk is a splendid emulsifying agent but is unsuitable for preparations which are to be kept over a considerable time unless preservatives be added.

Eggs have a considerable food value and are recommended as a source of the constituents of brain and nerve tissue. They are also high in protein and vitamins.

ALLIED DRUGS.—**Fresh Egg Yolk or Vitellus** (U. S. P. 1882 to 1905; N. F. 1916 to 1947; in culture media, N. F. 1936 to date); **Fresh Egg Albumin** (N. F. 1916 to 1936; in culture media, N. F. 1936 to date; as a reagent, U. S. P. 1894 to date; N. F. 1936 to date); **Egg Shell or Testa Ovi; Albumin Tannate or Albutannin** (U. S. P. 1926 to 1942). Albumin Tannate is a compound of albumin and tannic acid which is prepared by mixing aqueous solutions of egg albumin (10) and tannic acid (6.5), washing the precipitated albumin tannate and drying. Albumin tannate is used as an intestinal astringent. It is not dissolved in the stomach and in the intestines is slowly decomposed with the liberation of tannic acid. Average dose, 2 gm.

CLASS MAMMALIA, ORDER CETACEA, FAMILY PHYSETERIDÆ

This class is characterized by the females having milk-secreting mammæ to nourish their young. The body is generally clothed with hair, respiration takes place by means of lungs, the brain is well developed and the heart is divided into two auricles and two ventricles. The general structure is largely dependent upon habits. To this class belong all the warm-blooded quadrupeds, bats, seals, whales, apes and man.

The *Cetacea* or whales have the pelvis and posterior limbs atrophied and possess a fish-like body specialized for swimming and ending in a horizontal tail or fluke. The anterior limbs are modified into fins or flippers. The body possesses little or no hair. It is thought by some that whales are the descendants of the large prehistoric animals which once roamed the earth, and which escaped extinction by adapting themselves to life in the sea. This order includes the largest animals living on the face of the earth today. The order is usually divided into the toothless or baleen whales which yield whalebone and oil and the toothed whales, which include the sperm whale yielding spermaceti; also and the dolphins and porpoises.

SPERMACETI

Spermaceti or Cetaceum (U. S. P. 1820 to date) is a waxy substance obtained from the head of the sperm whale, *Physeter macrocephalus* Linné. The generic name *Physeter* is from the Greek, meaning a blowpipe, and refers to the spouting of the whale; *macrocephalus* is from the Greek, meaning a large head.

The sperm whale is the only representative of its genus. It is widely distributed in schools in tropical and subtropical seas, principally the Pacific and Indian oceans. This whale often attains a length of 20 meters. It has an enormous head, comprising about one-third of its body and up to 9 meters in circumference. Near the snout is a blowhole through which the sperm whale ejects water to a considerable height. Its lower jaw is provided with large conical teeth, while the upper jaw has no functional teeth. In front of the cranium is a large cavity which contains an oily fluid. After killing the animal, which is usually accomplished with torpedo harpoons which explode upon striking the animal, the cranial cavity is opened and the oily liquid transferred to barrels, a single whale yielding from 10 to 12 barrels of oil. On cooling, about 10 to 12 per cent of spermaceti separates out, which is removed by straining, and purified by compression and washing with weak, boiling alkali. The purified spermaceti is then allowed to cool and congeals into cakes.

DESCRIPTION.—A white, somewhat translucent, slightly unctuous mass having a crystalline fracture, and a pearly luster. It has a very faint odor, and a bland, mild taste. Consult the U. S. Pharmacopœia for standards and tests.

CONSTITUENTS.—Spermaceti consists almost entirely of cetyl palmitate, $C_{15}H_{31}COOC_{16}H_{33}$.

USES.—Spermaceti is an emollient and is used as a base for cerates and ointments.

ALLIED PRODUCTS.—**Ambergris** is a pathological product found in the intestine of the sperm whales or cast by them into the sea. It occurs in irregular grayish or brownish masses up to 75 kg. in weight. It contains a substance known as ambrein. Ambergris is high-priced and is used principally in perfumery as a fixative. It was at one time used as a stimulant and antispasmodic.

Whale Oil was at one time extensively used for illuminating purposes but upon the discovery of petroleum was replaced by kerosene. Numerous substances have also been invented to replace **whalebone**, so that the one-time large and flourishing whaling industry is now nearly extinct.

UNGUICULATA, ORDER CARNIVORA, FAMILY VIVERRIDÆ

The *Unguiculata* are the clawed mammals; the *Carnivora*, the flesh-eating animals with large projecting canine teeth; and the *Viverridæ* are the civet-cats and mongooses. The terrestrial carnivora also include dogs, foxes, raccoons, skunks, hyenas, cats, lions, etc.

Civetta or Civet is an unctuous secretion contained in a special pouch in both the male and female Civets, *Viverra civetta* and *V. zibetha*. The former is indigenous to Africa and the latter to southern Asia. These small cat-like carnivorous animals have short legs, a curly tail, a long body and a sharp snout. They are sometimes kept in captivity, the secretion being removed by means of a small spoon, a few cubic centimeters being obtained from each animal at intervals of a few days. The secretion is dried and at first is of a yellowish color, becoming dark brown; it has a strong musk-like odor, which becomes pleasant on dilution and is used both alone and for fixing other odors. The American civet-cat of Mexico is not a true civet, but is related to the raccoon and is similar in its haunts and habits to the latter.

UNGUICULATA, ORDER RODENTIA, FAMILY CASTORIDÆ

The rodents, or gnawing animals, include the hares, squirrels, gophers, mice, rats, guinea-pigs and beavers; the latter grouped into the family *Castoridæ*.

Castoreum or Castor (U. S. P. 1820 to 1882) consists of the dried preputial follicles of the beaver, *Castor fiber*, collected in Canada, the United States and Siberia. It contains a musk-like secretion used as a fixative in perfumery.

ORDER UNGULATA, FAMILY CERVIDÆ, SUBFAMILY MOSCHIDÆ

This is an order of mammals which are terrestrial and largely herbivorous. They have more or less hair and are characterized by having solid, tough, horny hoofs. The canine teeth are very small but the molars and premolars have broad crowns and are well adapted to chewing. The order is divided into four groups: (1) the *Artiodactyla* (with an even number of toes) like the hog, peccary, hippopotamus, camel, sheep, deer and cattle; (2) the *Perissodactyla* (with an odd number of toes) like the tapir, rhinoceros and horse; (3) the *Hyracoidea;* and (4) the *Proboscidea* or elephants. The sub-order *Artiodactyla* is sometimes divided into ruminants (those that chew the cud) and non-ruminants. The horse of the genus *Equus* (Fam. *Equidæ*) yields nothing directly to medicine, but is employed in the production of certain antibodies such as the antitoxins and antivenins, described on pages 74 to 76.

The family *Cervidæ* includes the deer, the principal characteristic of which are the antlers, present usually only in the male. Some authors consider the musk-deer as a sub-family, while others classify it as a distinct family.

The *Moschidæ* includes the small hornless deer having a short tail. The canine teeth are well developed and in the male project from the upper jaw. The musk deer is important as the source of musk which, while not official, is nevertheless an important and valuable article.

Moschus or Musk (U. S. P. 1820 to 1926) is the dried secretion from a special follicle of *Moschus moschiferus*. The musk deer inhabits the mountainous regions of the northern provinces of China, Tibet and Siberia, extending to the elevated tablelands of the Balkan Sea. The musk sac is found only in the buck deer and is located on the abdomen between the umbilicus and the preputial follicle. The animals are hunted in the spring and early summer and killed. The musk sac is removed as quickly as possible and carefully dried, the sacs of animals about six years old being preferred. They are placed in small, rectangular cases (Catties) lined with tinfoil, shipped to Shanghai and then exported to Europe.

The musk sac is nearly ovoid and from 4 to 7 cm. in length, the upper surface being smooth, the lower convex and covered with grayish brown hairs, which are concentrically arranged around a small orifice. The secretion in the fresh state is of an unctuous consistence; it dries in the form of irregular granules from 1 to 2 mm. in diameter, of a light brown or brownish black color, being shiny and somewhat oily, having a peculiar penetrating and persistent odor and an aromatic, bitterish taste.

Upon the addition of a few grains of musk to 2 cc. of chloroform in a watch crystal the grains float on the surface. Upon stirring with a glass rod, the solution remains nearly colorless and as it evaporates there separates, around the particles, a small quantity of a whitish oil or fatty substance.

The amount of musk soluble in water varies from 50 to 75 per cent. The aqueous solution should be of a dark brown color, having a strongly aromatic odor and a slightly acid reaction. The undissolved portion consists of irregular fragments containing a finely granular substance; in addition there are numerous rod-like bacteria held in suspension and occasionally the hyphæ of a fungus.

The amount of musk soluble in alcohol should not be less than 10 per cent. The solution should be of a light yellowish brown color and should become slightly turbid upon the addition of water.

Musk contains from 0.5 to 2 per cent of a colorless, viscid volatile oil, consisting of a ketone having the odor of musk. Also fat, resin, cholesterin, protein substances, ammonium salts, calcium salts and about 5 per cent of ash. Musk should not lose more than 15 per cent of moisture when dried in a desiccator over sulfuric acid.

Musk is sometimes adulterated with dried blood, colophony, catechu, asphalt, glass, sand, meat, small seeds and fragments of wood, all of which are readily detected.

Moschus is said to be a nervine and an antispasmodic. It produces a very strong perfume and is used as a fixative in perfumes. It is now rarely obtained and is so constantly adulterated and high-priced that its use is restricted. Average dose, 0.25 gm.

FAMILY BOVIDÆ

This is a family of ruminating mammals possessing hollow, unbranched horns. To this family belong the sheep, antelope, ox, buffalo and bison. Two animals, the sheep (*Ovis aries*) and the ox (*Bos taurus*) are of interest as sources of drugs.

The sheep was probably the first animal domesticated by man. Its wool constitutes one of our most important textile fibers and supplies a large part of the clothing of man. Leather made from the skin is used in bookbinding and for making gloves. The intestines are used as sausage casings and also supply catgut used for ligatures and as strings for musical instruments. The meat of the sheep known as mutton is an important article of food. Among the drugs yielded by the sheep are the fat of the wool, known as wool fat, the abdominal fat, known as suet, and many glandular products. Sheep are widely bred in the temperate zones, the United States having approximately 50,000,000.

The term cattle is applied to domesticated bovine animals of which there are two principal species, *Bos taurus*, including the European cattle, and *Bos indicus* the humped cattle of India and Africa, the latter known as Zebu. American cattle are descendants of cattle imported largely from Great Britain. Our cattle have been extensively bred with two objects in view, that of producing flesh (Beef cattle) and that of increasing lactation (Dairy cattle). Most of the pharmaceutical products yielded by cattle are collected at the time of slaughter, purified and preserved according to their nature. Among these products are oxgall, and glandular substances. Cattle, together with sheep and hogs, are the source of such important enzymes as pepsin and pancreatin and the extensively used endocrine products. The student is also referred to the preparation of smallpox vaccine (see page 67), which is prepared upon living calves.

PREPARED SUET

Prepared Suet or Mutton Suet (U. S. P. 1820 to 1947; N. F. 1947 to date) is the internal fat of the abdomen of the sheep, *Ovis aries* Linné, purified by melting and straining. The generic name *Ovis* is the Latin word for sheep and *aries* is Latin for ram. The internal fat of the abdomen removed during slaughtering is comminuted, mixed with water, heated to about 65° C. (when the melted suet rises to the top), separated, strained and allowed to cool and congeal.

Description.—Prepared suet is a white, solid fat, having, when fresh, a slight, characteristic odor and bland taste. It becomes rancid on prolonged exposure to air and must not then be used. Consult the National Formulary for its solubility.

Constituents.—Prepared suet contains from 70 to 80 per cent of stearin and palmitin and from 20 to 30 per cent of olein.

Standards and Tests.—Prepared suet melts between 45° and 50° C. and congeals between 37° and 40° C.; its saponification value is not less than 193 and not more than 200; its iodine value is not less than 33 and not more than 48, and the fatty acids in 10 gm. require not more than 6 cc. of tenth-normal sodium hydroxide for neutralization.

Uses.—Prepared suet is an emollient. It enters into certain ointments, where it is stiffer than lard.

Stearic Acid (U. S. P. 1894 to date) is a mixture of solid acids obtained from fats, and consists chiefly of palmitic acid, $CH_3(CH_2)_{14}COOH$, and stearic acid, $CH_3(CH_2)_{16}COOH$.

Stearic acid is usually prepared from mutton or beef tallow. The fat is saponified, the soap treated with an acid and the liberated fatty acids pressed to remove the liquid oleic acid. Consult the Pharmacopœia for the characters and tests of stearic acid. It is used in the manufacture of glycerin suppositories (as sodium stearate) and for certain skin affections (as zinc stearate).

Oleic Acid (U. S. P. 1882 to date) is a liquid acid obtained from tallow and other fats, consisting chiefly of $CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH$.

As mentioned above, oleic acid is obtained as a by-product in the manufacture of stearic acid. It is also obtained from certain fixed oils, notably almond oil. Consult the Pharmacopœia for characters and tests. Oleic acid is largely used in the preparation of oleates.

WOOL FAT

Wool Fat or Anhydrous Lanolin (U. S. P. 1905 to date) is the purified, fat-like substance from the wool of the sheep, *Ovis aries* Linné. Wool contains up to 50 per cent of a fat-like or waxy substance known as **suint** which is removed by washing the wool with benzin or other cheap solvent or by treatment with soap solution. It is then collected, strained, purified, bleached and finally dehydrated. The processes for these steps are either secrets or covered by patents.

Description.—Wool fat is a brownish yellow, tenacious, unctuous mass, having not more than a slight odor. Wool fat is insoluble in water, but can be mixed, without separation, with about twice its weight of water. It is sparingly soluble in cold alcohol, more soluble in hot alcohol and freely soluble in ether and in chloroform.

Constituents.—The chief constituents are cholesterol, $C_{27}H_{45}OH$, and isocholesterol. Wool fat also contains the esters of lanopalmitic, lanoceric, carnaubic, oleic, myristic, and other fatty acids.

Cholesterol may be demonstrated by dissolving 0.5 gm. of lanolin in 5 cc. of chloroform and adding 1 cc. of acetic anhydride and 2 drops of sulfuric acid: the mixture will acquire a deep green color.

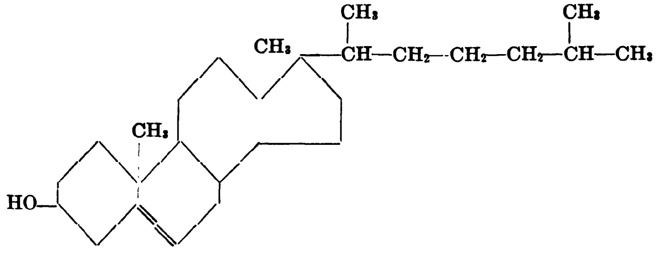
Standards.—Wool fat melts between 38° and 42° C.; it contains not more than 0.5 per cent of water and not more than 0.1 per cent of ash and is free from alkalis, chloride, glycerin, soluble oxidizing impurities and petrolatum. Consult the U. S. Pharmacopœia for methods.

Uses.—Wool fat is an emollient and a base for creams and ointments. It is more readily absorbed through the skin than any other known fat and is therefore valuable as a base for mercury and other remedies which are to be administered by inunction.

Hydrous Wool Fat or Lanolin (U. S. P. 1894 to date) is wool fat containing not less than 25 per cent and not more than 30 per cent of water. Consult the U. S. Pharmacopœia for its characters and tests. It is used as a vehicle for the external administration of remedies locally or by inunction.

STEROLS

The sterols comprise a large group of substances occurring in plants and animals. They are usually associated with fats and are found in the unsaponifiable portions of those fats. They differ little in structure all having the cyclopentanophenanthrene nucleus to which a hydroxyl group is attached at position 3, methyl groups at 10 and 13 and a side chain at 17. Double linkages may be present in the side chain, in the cyclic system, or in both. Cholesterol, the most common of the sterols has the following formula:



Many therapeutic agents of rather widely different therapeutic activity are, or contain, sterols. Among these may be mentioned:

Ergosterol, which when irradiated becomes Calciferol or vitamin D_2, and also vitamin D_3 which is 7-dehydrocholesterol.

The Bile Acids, including taurocholic, glycocholic and cholic.

The Estrogens, including Estrone, Estriol and Estradiol.

The Androgens, including Testosterone and Androsterone. (These are sterones in which an —OH group becomes an O.)

The Adrenal Cortex Hormones. (see page 708).

The Digitalis Aglycones, such as Digitoxigenin obtained upon the hydrolysis of Digitoxin.

Cholesterol or Cholesterin (U. S. P. 1947 to date, N. F., as a reference standard. 1936 to date) comprises the larger part of Lanolin and is found in many other drugs.

The Saponins.—Some of the aglycones of the saponins have been shown to possess the cyclopentanophenanthrene nucleus.

OX BILE

Ox Bile or Oxgall (U. S. P. 1882 to 1947; N. F. as a reagent, 1942 to date; U. S. P. as purified oxgall, 1882 to 1916; as inspissated oxgall 1882 to 1894) is the fresh bile of *Bos taurus* Linné. The generic name *Bos* is from the Latin *bovis* or the Greek *bous* meaning ox; *taurus* (or Greek *tauros*) means a bull. Bile is a natural secretion of the liver which during life passes into the intestinal tract where it aids in the digestive processes by emulsifying fats, promoting peristalsis and absorption, and preventing putrefactive changes.

Description.—A brownish green or dark green, somewhat viscid liquid, having a characteristic odor, and a disagreeable, bitter taste. The specific gravity ranges between 1.015 and 1.025 at 25° C. Ox bile is neutral or slightly alkaline to litmus.

Constituents.—Ox bile contains from 80 to 90 per cent of water and from 10 to 15 per cent of total solids consisting principally of the sodium salts of glycocholic and taurocholic acids known commonly as "bile salts." Glycocholic acid hydrolyzes into cholic acid and glycine while taurocholic acid hydrolyzes into cholic acid and taurin. Ox bile also contains the bile pigments bilirubin and biliverdin, and small quantities of cholesterin, choline, fat, albumin, mucin and urea.

TESTS.—Of particular interest is the official test (Pettenkoffer's reaction) which is carried out as follows: 2 drops of ox bile are mixed with 10 cc. of water and a drop of freshly prepared solution of 1 part of sucrose in 4 parts of water. Sulfuric acid is cautiously added until the precipitate first formed is redissolved: the mixture gradually acquires a brownish red color, changing successively to carmine, purple and violet. The violet color is due to the reaction between cholic acid, formed from the hydrolysis of the bile acids, and furfuraldehyde formed by the action of the acid on the sucrose.

Ox Bile Extract or Powdered Oxgall Extract (U. S. P. 1916 to date) is prepared by partial evaporation of fresh ox bile, precipitation of the mucus and albuminous matter with alcohol, filtering, washing and evaporating the combined filtrates to dryness at a temperature not exceeding 80° C. The resulting extract is powdered and sufficient starch added so that 1 gm. of the extract represents 8 gm. of ox bile.

USES AND DOSE.—Ox bile is a cholagogue, a laxative and an intestinal antiseptic. It is usually given when biliary secretion seems deficient Average dose, 0.4 gm.

MILK

Cow's Milk (N. F. 1916 to 1942; in culture media N. F. 1942 to date) is the fresh, unpasteurized or pasteurized milk of *Bos taurus* Linné, without modification, and complying with the legal standards of the state or community in which it is sold.

Cow's milk is a white, opaque liquid, being an emulsion of minute fat globules suspended in a solution of casein, albumin, lactose and inorganic salts. It has a slight but pleasant odor and an agreeable sweetish taste. Cow's milk has a specific gravity between 1.029 and 1.034 and contains from 80 to 90 per cent of water in which are dissolved about 3 per cent of casein, about 5 per cent of lactose and from 0.1 to 1 per cent of mineral salts. Milk contains from 2.5 to 5 per cent of fat (butter) and is rich in vitamins. When milk is allowed to stand a few hours the fat globules (cream) rise to the top. Each is surrounded by an albuminous layer. Upon churning, the fat globules unite to form **butter**, leaving a liquid known as **buttermilk.** The milk left after separation of the cream is known as **skimmed milk,** which if treated with rennin (see below) forms a coagulum which upon proper treatment is made into **cheese.** The liquid separated from the coagulum is known as **whey** and contains lactose and inorganic salts.

Milk is a nutrient. It is the source of lactose and kumyss.

Lac Fermentatum (N. F. 1916 to 1936), **Fermented Milk or Kumyss,** is prepared by dissolving 35 gm. of sucrose in 1 liter of milk and fermenting with compressed yeast. Fermented milk is more readily digested and absorbed than milk. It is used as a nutrient especially in cases of stomach irritability. **Condensed Milk** is prepared by partial evaporation of milk in a vacuum, and sterilization in hermetically sealed containers by autoclaving. **Malted Milk** is prepared by evaporating milk with an extract of malt. Low heat and vacuum are used so as not to destroy the enzymes present.

Casein (U. S. P. 1926 to date; and N. F. 1936 to date, as culture media) and **Sodium Caseinate or Nutrose** (N. F. 1942 to date, as culture media) are extensively used.

Lactose or Milk Sugar $C_{12}H_{22}O_{11}.H_2O$ (U. S. P. 1863 to date; N. F. 1926 to date, in culture media), is a sugar obtained from milk. The sugar is crystallized from the whey obtained in cheese manufacture.

These impure crystals are redissolved in water, decolorized with charcoal and recrystallized.

DESCRIPTION.—Lactose is odorless and has a faintly sweet taste. It is stable in air but readily absorbs odors. Upon hydrolysis lactose yields β-glucose and β-galactose. It reduces Fehling's solution, undergoes mutarotation and forms an osazone (see page 113). Lactose is hydrolyzed by the specific enzyme lactase. It is not hydrolyzed by maltase, sucrase or diastase and differs markedly from the other sugars in the great ease with which it undergoes lactic and butyric acid fermentations.

STANDARDS AND TESTS.—Lactose should be free from dextrose, sucrose, dextrin, starch and heavy metals. Consult the U. S. Pharmacopœia for constants, etc.

USES.—Lactose is less sweet than sucrose and is more easily broken down. It is used therefore as a nutrient in infants' food. Its principal pharmaceutical use is that of an inert diluent for other drugs.

Galactose (N. F. 1936 to date, in culture media) is obtained upon hydrolyzing lactose. **Dulcitol** (N. F. 1936 to date, in culture media) is obtained by reducing galactose.

Lactic Acid ($CH_3.CHOH.COOH$) (U. S. P. 1863 to 1947; N. F. 1947 to date) is a mixture of lactic acid and lactic anhydride equivalent to a total of not less than 85 per cent and not more than 90 per cent of $HC_3H_5O_3$. Lactic acid is prepared by the action of the special lactic ferment (*Bacterium lactis*) on lactose, invert sugar, milk or cheese, the lactic acid formed being neutralized with chalk or zinc oxide. The calcium or zinc lactate is recrystallized and decomposed with acid. Consult the National Formulary for the properties and tests of lactic acid. Lactic acid is a caustic, a hypnotic and a stomachic.

BEEF

Extract of Beef (N. F. 1926 to date; in culture media U. S. P. 1916 to 1926; N. F. 1926 to date and U. S. P. 1942 to date) is a residue from beef broth, obtained by extracting fresh, sound, lean beef by cooking with water, adding salt, and evaporating the broth at a low temperature, usually in a vacuum, until a thick pasty residue is obtained.

DESCRIPTION.—Extract of beef is a yellowish brown to dark brown, slightly acid, pasty mass having an agreeable meat-like odor and taste.

CONSTITUENTS.—Extract of beef contains creatine creatinine carnine carnic acid and xanthine. It is less nutritious than meat as fat, albumin, gelatin and fibrin are removed in the process of manufacture.

STANDARDS AND TESTS.—Extract of beef should yield not less than 75 per cent of total solids; the ash should not exceed 30 per cent of the total solids, and the sodium chloride, in the ash, should not exceed 10 per cent of the total solids; the alcohol-insoluble (2 vol. alcohol and 1 vol. water) solids do not exceed 10 per cent of the total solids; 1 gm. of the alcohol-soluble solids yields not less than 60 mg. of nitrogen. The amount of ammonia does not exceed 0.35 per cent of the total solids; extract of beef should be free from nitrate. Consult the National Formulary for tests and methods.

USES.—Extract of beef is a nutrient. It is used in preparing the official Elixir of Beef and Iron.

Aminoacetic Acid, Glycocoll or Glycine (U. S. P. 1942 to 1947; N. F. 1947 to date) is employed as a nutrient.

Beef products used in the preparation of culture media include: **Beef** (N.F. 1942 to date): **Veal** (N. F. 1926 to date); **Beef Heart** (N. F. 1936 to date); **Beef Liver** (N. F. 1942 to date); **Calf's Brain** (N. F. 1936 to date); **Blood** (U. S. P. 1936 to 1942 and N. F. 1936 to date); **Dried Blood Serum** (N. F. 1926 to date) and **Ascitic Fluid** (N. F. 1936 to date). **Peptone** is extensively used in culture media (U. S. P. 1916 to 1926 and 1936 to date, N. F. 1926 to date). **Creatinine** is employed as a reference standard (N. F. 1947 to date).

ALLIED DRUGS.—Among other drugs yielded by *Bos taurus*, the following might be mentioned. **Oleum Bubulum or Neat's Foot Oil** (U. S. P. 1831 to 1873) is a fixed oil obtained by boiling the fatty tissue of the feet of the ox (deprived of the hoofs) in water, and skimming off the oil. It is yellowish, has a peculiar odor and is used for softening leather. **Sanguis or Blood,** is the arterial blood of the ox. When evaporated to dryness, it yields **Extractum Sanguis, Pulvis Sanguis or Dried Blood,** which has been used as a restorative.

ENZYMES

Enzymes are organic catalysts produced by living organisms. They make possible the many complex chemical reactions which make up life processes. Although produced by living organisms, they are themselves lifeless. They may be isolated and when so obtained still exert their characteristic catalytic effect. While very little is known regarding their chemical constitution, they do exhibit several properties in common: they are colloids and are soluble in water and dilute alcohol but are precipitated by concentrated alcohol; most enzymes act best at temperatures between 35° and 40° C.; temperatures above 65° C. especially in the presence of moisture, usually completely destroy them while at 0° their activity is negligible; certain heavy metals, formaldehyde and free iodine retard their activity. Their activity is markedly affected by the pH of the medium in which they act or by the presence of other substances in this medium; and they are usually highly selective in their action. Some of the enzymes have been demonstrated to be proteins although very little is known concerning their chemical constitution. They are therefore usually classified as to their selective action; thus, amylolytic, proteolytic and lipolytic are enzymes which split starch, proteins and fats respectively. They may also be classified according to the type of chemical change which they accelerate, such as hydrolysis, fermentation or oxidation, thus invertase hydrolyzes starch; lipase, fats; and pepsin, proteins; while zymase is a typical fermenting enzyme. Enzymes often occur in combination with inorganic or organic substances that accelerate their action. These substances are known as co-enzymes and it has recently been shown that the co-enzymes are integral components of a large number of enzyme systems. Several vitamins (vitamin B_1, riboflavin and nicotinic acid) are recognized as having a co-enzymatic function.

The nomenclature of enzymes is variable, though the terms used to designate enzymes usually end in *ase* or *in*. The more important and better known enzymes are presented as follows:

I. The **Amylolytic** enzymes or **Carbohydrases**

Diastase (U. S. P. 1916 to 1926), together with **amylase**, terms applied to several well-known amylolytic enzymes. Salivary diastase, or **ptyalin** and pancreatic diastase or **amylopsin** are enzymes found in the digestive tract of animals. **Malt diastase** is formed during the germination of barley grains. Diastase converts starch into maltose. It is most active in solutions which are approximately neutral, a reaction of pH 4 destroying the enzyme.

Invertase or Sucrase, is found in yeast, and in the intestinal juices. It brings about the hydrolysis of sucrose into glucose and fructose. **Maltase** which causes the conversion of maltose into glucose is also found in yeast and the intestinal juices.

Zymase is a fermenting enzyme causing the breaking up of monosaccharides (glucose, fructose) into alcohol and carbon dioxide.

Emulsin is an enzyme found in almonds. It causes the hydrolysis of beta-glycosides; thus amygdalin is hydrolyzed into glucose, benzaldehyde and hydrogen cyanide.

Myrosin is found in white and black mustard and hydrolyzes sinalbin and sinigrin as well as other glycosides.

II. The **Esterases** include those enzymes that split esters. The group includes the *liptolytic* enzymes.

Lipase is a lipolytic enzyme widely distributed in the animal and vegetable kingdoms. It is found in the pancreatic juice of animals and in the oily seeds. Lipase causes the hydrolysis of fats into glycerin and fatty acids.

Pectase will split pectin into pectic acid and methyl alcohol.

Urease (N. F. 1936 to date), obtained from soy beans, is used as a laboratory reagent for converting urea to ammonia.

III. The **proteolytic** enzymes

Pepsin is a proteolytic enzyme found in the gastric juice. It operates best at a pH of about 1.8 and in neutral or alkaline media is entirely inactive. It converts proteins into proteoses and peptones.

Trypsin is formed from the pro-enzyme or zymogen, trypsinogen, when acted upon by the enterokinase of the intestinal juices. Trypsinogen is found in the pancreatic juice. Trypsin is a proteolytic enzyme which is considerably more active than pepsin, converting proteoses and peptones into polypeptids and amino acids. It acts best in an alkaline medium of about pH 8, and may thus be distinguished from pepsin which acts only in acid media.

Erepsin is a proteolytic enzyme also found in the intestinal juices. It converts proteoses and peptones into amino acids.

Rennin is a coagulating enzyme present in the mucous membrane of the stomach of mammals. It curdles the soluble caseinogen of milk.

Papain is a mixture of active proteolytic enzymes found in the unripe fruit of the pawpaw tree (see page 443). Among the enzymes present in **Papain** is **Peptidase I** which converts proteins into polypeptides and dipeptides.

IV. The **oxidizing** enzymes

Peroxidases are found widely distributed in plants. They bring about the oxidation reactions which cause the discoloration of fruits upon bruising.

Thrombin converts the fibrinogen of the circulating blood into the insoluble fibrin of the blood clot.

Zymase, although splitting monosaccharides, is essentially an oxidizing enzyme, since the monosaccharide is split by oxidation.

Enzymes, as a group, have been discussed at this point because of their connection with the three following drugs, Rennin, Pepsin and Pancreatin.

RENNIN

Rennin (N. F. 1916 to date) is the partially purified milk-curdling enzyme obtained from the glandular layer of the stomach of the calf, *Bos taurus* Linné. Rennin may be prepared by macerating the minced glandular layer of the digestive stomach of the calf in 0.5 per cent sodium chloride solution, filtering, acidifying the filtrate with hydrochloric acid and saturating it with sodium chloride. The enzyme is precipitated by the sodium chloride, separated, dried and powdered. In commerce it is prepared by a variety of processes which are more or less trade secrets.

DESCRIPTION.—Rennin occurs as a grayish white or yellowish white powder, or as pale yellow grains or scales, having a characteristic and slightly saline taste, and a peculiar, not unpleasant odor.

STANDARDS AND TESTS.—Rennin possesses a coagulating activity of not less than 90 per cent and not more than 110 per cent of the Reference Rennin. (Reference Rennin is a carefully preserved, stable, powdered rennin that has been repeatedly tested for a number of years so that its stability and its standard are definitely established. It is used as a reference standard in the rennin assay on the basis of coagulating approximately, but not less than, 25,000 times its own weight of fresh cow's milk.) Rennin of a higher coagulating power may be brought to the requisite strength by admixture with lactose and sodium chloride. It shows no cellular structure upon microscopic examination and no blue color upon the addition of iodine T.S.

USES.—Rennin is used to coagulate milk, thus preparing it as a food for convalescents. It is also used as a digestant in the official Elixir of Pepsin and Rennin. Its principal use, however, is to coagulate milk for the manufacture of cheese.

SUIDÆ OR SWINE FAMILY

This family includes the non-ruminating cloven-hoofed ungulates having a thick skin bearing bristle-like hairs and having incisor, canine, premolar and molar teeth in both jaws. They have no horns. The domesticated races are called hogs.

PEPSIN

Pepsin (N. F. 1888 to 1896; U. S. P. 1894 to 1942; N. F. 1942 to date) is a substance containing a proteolytic enzyme obtained from the glandular layer of the fresh stomach of the hog *Sus scrofa* var. *domesticus* Gray. The generic name *Sus* is from the Greek *Us* meaning hog; *scrofa* is Latin for breeding sow; and *domesticus* is from the Latin meaning the household.

Pepsin is prepared by digesting the minced stomach linings with hydrochloric acid. This solution is clarified, partially evaporated, dialyzed, concentrated and either poured on glass plates to dry, thus forming **scale pepsin** or carefully evaporated in a vacuum to form **spongy pepsin.**

DESCRIPTION.—Pepsin occurs in lustrous, transparent or translucent scales, or in granular or spongy masses ranging in color from light yellow to light brown, or a fine white or cream-colored amorphous powder, free from offensive odor, and having a slightly acid or saline taste. Consult the National Formulary for further properties and identity tests.

STANDARDS.—Pepsin digests not less than 3000 and not more than 3500 times its weight of egg albumin. A pepsin of higher digestive power may be reduced to the official standard by admixture with a pepsin of lower power or with lactose. In this connection it is interesting to note that pepsin as produced commercially (especially spongy pepsin) often runs from four to five times the official requirement.

USES AND DOSE.—Pepsin is administered to assist gastric digestion. It should be given after meals and followed by a dose of hydrochloric acid. Average dose, 0.5 gm.

PANCREATIN

Pancreatin (N. F. 1888 to 1896; U. S. P. 1894 to date) is a ubstance, containing enzymes, principally amylase, trypsin and lipase, obtained from the fresh pancreas of the hog, *Sus scrofa* Linné var. *domesticus* Gray or of the ox, *Bos taurus* Linné. The pancreas is a gland lying just inside the posterior wall of the abdomen. The fresh glands are minced and extracted by methods similar to those employed in the manufacture of pepsin. As is the case with pepsin and rennin, the methods used for obtaining pancreatin are especially developed and carefully kept secret by the manufacturers.

DESCRIPTION.—Pancreatin is a cream-colored amorphous powder having a faint, characteristic, but not offensive odor. Its greatest activity is in neutral or faintly alkaline solution. More than traces of mineral acids or large amounts of alkali hydroxides render it inert and an excess of alkali carbonates inhibits its action. Consult the U. S. Pharmacopœia for its properties and tests.

CONSTITUENTS.—Pancreatin contains three enzymes, amylopsin (amylase), trypsin and steapsin (lipase). The action of these enzymes as well as those of rennin and pepsin are discussed in the section on Enzymes, page 689.

USES AND DOSE.—Pancreatin is used as a digestant and in the preparation of pre-digested foods for invalids. Recently, enteric-coated granules of Pancreatin have been used in treating infants with celiac disease and related pancreatic deficiencies. Average dose, 0.5 gm.

LARD

Lard (U. S. P. 1820 to date) is the purified internal fat of the abdomen of the hog, *Sus scrofa* Linné var. *domesticus* Gray. The fat from the mesentery, omentum and kidneys is separated from blood-vessels and adhering tissue. This is cut into small pieces and melted in steam kettles at a temperature usually not exceeding 57° C. The melted fat is washed with water and after rising to the top is run off, dried with low heat, strained and allowed to solidify.

DESCRIPTION.—Lard is a soft, white, unctuous mass, having a faint odor, and a bland taste. It is free from rancidity, melts at 36° to 42° C., forming a clear liquid from which no aqueous layer separates. It has a saponification value of not less than 195 and not more than 203 and an iodine value of not less than 46 and not more than 70. Consult the U. S. Pharmacopœia for further properties and requirements.

CONSTITUENTS.—Lard contains about 60 per cent of olein and about 40 per cent of myristicin, stearin and palmitin. The olein being liquid may be separated by pressure at 0° C., and when so separated is known as **lard oil.** The solid mixture of myristicin, stearin and palmitin is sold as **stearin.**

STANDARDS.—Lard should be free from water, chlorides, cottonseed fats and beef stearin. Consult the U. S. Pharmacopœia for methods of detection.

USES.—Lard is an emollient and is used as a base for ointments and cerates. It has a tendency to become rancid and is often combined with 1 per cent of Siam benzoin (see **Benzoinated Lard**), (U. S. P. 1863 to date).

Lard Oil (U. S. P. 1882 to 1916) is an oil consisting mainly of olein, expressed from lard and used chiefly as a lubricant and illuminant.

GELATIN

Gelatin (U. S. P. 1905 to date; in culture media N. F. 1926 to date; as a reagent U. S. P. 1894 to date and N. F. 1936 to date) is a product obtained by the partial hydrolysis of collagen, derived from the skin, white connective tissue, and bones of animals. Commercially, gelatin is prepared from the suitable by-products of slaughtered cattle, sheep and hogs. Bones are first decalcified by treatment with hydrochloric acid. The materials are extracted with boiling water and steam under pressure until the collagen is hydrolyzed. The solution is then filtered by electro-osmosis, concentrated under reduced pressure, allowed to jell and rapidly dried on netting in currents of warm air.

Description.—Gelatin occurs in sheets, flakes, shreds or as a coarse or fine powder. It is colorless or yellowish and has a very slight, characteristic odor and taste. When dry it is stable in the air, but when moist or in solution it is subject to bacterial decomposition. Gelatin is insoluble in cold water but swells and softens when immersed in it, gradually absorbing from 5 to 10 times its weight of water. It is soluble in hot water, insoluble in most immiscible solvents and in volatile and fixed oils. An aqueous solution of gelatin (1 to 100) yields precipitates with chromium trioxide and trinitrophenol solutions but none with solutions of cupric sulfate or mercuric chloride.

Constituents.—Gelatin contains a gelatinizing substance known as chondrin and small quantities of an adhesive substance known as glutin.

Standards and Tests.—The Pharmacopœia requires that a 1 per cent gelatin solution form a non-flowing jelly at 10° C. when prepared as directed. A hot solution (1 to 40) should be free from putrid odor. Gelatin must meet the pharmacopœial limits on heavy metals, arsenic and sulfur dioxide.

Uses —Gelatin is a nutrient. It is used pharmaceutically for pill coating and capsule manufacture. Combined with glycerin to form the official glycerinated gelatin, it is employed as a vehicle and for the manufacture of suppositories. It is extensively used for the preparation of bacteriological culture media.

Allied Products.—**Glue** is prepared in a somewhat similar manner to gelatin. The gelatinizing power (chondrin) is, however, destroyed by treatment with acids leaving the adhesive glutin.

Keratin or Ceratin is a substance somewhat resembling protein except that some of the oxygen is replaced by sulfur. It is found in cattle and horses' hoofs, feather quills, finger-nails, etc. It is prepared from horny substances by digesting with pepsin to remove all substances soluble in gastric juice, taking up in ammonia, filtering and evaporating. Keratin occurs in yellowish thick scales which are soluble in alkalis and strong acetic acid but insoluble in water and dilute acids. It has been used as an enteric coating for pills and tablets.

Cornu Cervi or Hartshorn (U. S. P. 1820 to 1842) consists of the horns of the stag deer boiled to remove gelatin and the clean horns incinerated, resulting in an almost pure calcium phosphate. It is of historical interest since it was an ingredient of our first antimonial, James' Powder.

Os or Bone (U. S. P. 1831 to 1882) consists of the bones of vertebrate animals which are composed of cellular gelatinous tissue filled with calcareous deposits. Its principal use is for preparing animal charcoal (boneblack). Being high in phosphates, it is often ground (bone-meal) and used as fertilizer.

PURIFIED ANIMAL CHARCOAL

Purified Animal Charcoal (U. S. P. 1831 to 1916, as Animal Charcoal; U. S. P. 1842 to 1916 as Purified Animal Charcoal; N. F. 1926 to date) is charcoal prepared from bone and purified by removing the substances which are dissolved by hot hydrochloric acid and water. Bones are boiled in water to remove fat and then heated in iron cylinders without access of air. The charcoal thus obtained is boiled with hydrochloric acid, thoroughly washed and dried.

DESCRIPTION.—Purified animal charcoal is a dull black, amorphous, odorless and tasteless powder, which burns with a red glow but without a flame.

CONSTITUENTS.—Purified animal charcoal consists principally of carbon in such a form as to exhibit high adsorptive power.

STANDARDS AND TESTS.—Purified animal charcoal should yield not more than 4 per cent of ash and not more than 12 per cent of water. It must meet the requirements of the National Formulary for complete carbonization, impurities soluble in hydrochloric acid and adsorptive power.

USES.—Purified animal charcoal is used because of its high adsorptive power. For internal use it is usually compressed into tablets where it functions in the adsorption of gases. It is frequently administered in poisoning by alkaloids, heavy metals, etc. Large quantities are used for industrial purposes in the adsorption of coloring matter and the clarification and decolorizing of such products as sugar.

ENDOCRINE PRODUCTS

By an endocrine, or "ductless" gland, we mean a secreting organ, present in the mammalian body, which elaborates one or more metabolically active principles (hormones) and passes these directly to the blood stream. In some instances, mixed glands (pancreas, liver) also serve exocrine functions in passing secretions into hollow organs by means of duct systems.

The hormones so elaborated exert profound and essential influences regulating processes of metabolism, general growth and development, and the growth, development and function of the organs and characteristics of sex and reproduction. The word "hormone" infers an excitation—occasionally, the inhibitory principles are described as "chalones." This distinction is not generally observed.

Most of our present knowledge of endocrine function and therapy is the result of intensive investigations of the past forty years. In spite of the tremendous progress made to date, the picture is yet far from completion, and a rational basis for endocrine therapy cannot be established in all cases. Early therapy made use of dried glandular products, and of crude extracts prepared from them; wherever possible, therapy has been improved by the isolation of active principles, and by the synthesis of these and of related compounds modifying or extending the action of the native hormones. Products at present available for endocrine and hormonal therapy are therefore derived from:

1. By-products in the slaughter-house processing of cattle, hogs, and sheep. From these, powdered glands, gland extracts, and purified hormones have been prepared.
2. Synthetic products which duplicate (epinephrine, thyroxin), or closely mimic (stilbestrol, hexestrol, dihydrotachysterol) the actions of natural hormones.

Historical.—Our present endocrine therapy is the outgrowth of the more primitive practice of Organotherapy; therapy with organ products or extracts. Primitive medicine men of all ages have used the organs of strong animals to remedy diseases of those organs in man—the doctrine that "lung cures lung" so well expressed by Vicary who in the sixteenth century said, "In what part of the body the faculty which you would strengthen lies, take the same part of the body of another creature in whom the faculty is strong, as a medicine." An outstanding example of this is the use of human skull in epilepsy, extolled by Paracelsus in the sixteenth century. Oddly enough, the use of toad skins in early Chinese medicine has received modern support in the finding of epinephrine-like and digitalis-like principles in these skins. The use of powdered hog testis in male impotence, and the use of rabbit uterus in treating female sterility, by Magnus in the thirteenth century, are more nearly related to our present endocrinology.

General Considerations.—It should be borne in mind that the various endocrine glands function in close harmony, correlated with the more immediate functions of the central and autonomic nervous systems. For study, some isolation is necessary, yet artificial. It is obvious then that a primary focus of disturbance will have far-reaching influence, and as a result of this, an irrational use of complex products is frequently observed.

Disturbance in the function of an endocrine gland may take the form of excessive activity (hyperfunction), or diminished activity (hypofunction), to any degree. In the treatment of such disturbances, we must look upon the endocrine products as drugs, use of which should be based upon sound, rational considerations. The following points should be noted in summary:

1. Microscopy of glandular products is not too feasible. The fresh glands do not enter the general market; in the preparation of powders and extracts, most of the histologic features are lost. Standardization is usually effected by means of biologic assay; with the development of pure principles, there is increasing use of chemical means of assay, and a commendable tendency to substitute weight units for assay units in dosage.
2. The hormones are not species specific. Thus, products obtained from domesticated food animals are effective in treating diseases in man. Such therapy does not always bear out the predictions of physiologic investigation, due among other things to a frequent inability to limit action, or to control side effects.
3. Hormones do not "excite" or "cure" a diseased gland. Therapeutic use depends essentially upon two types of action:
   (*a*) Replacement of existing deficiency.
   (*b*) Pharmacologic action upon non-endocrine structures.

Replacement therapy is applied to the relief of symptoms resulting from glandular hypofunction. In such use, early diagnosis and treatment are essential in avoiding irreversible changes which may occur, as in cretinism, giantism, and other conditions. Therapy must consider the possible danger of side-effects, and of profound, widespread alterations in body function.

The Pancreas, and Insulin Products

The bulk of the pancreas is an exocrine gland, supplying digestive enzymes to the duodenum. Isolated groups of cells, the islets of Langerhans comprising about 3 per cent of the gland, produce the hormonal function inherent in preparations of Insulin. This hormone known as insulin:

1. Functions as a necessary factor in the cellular oxidation of glucose, and secondarily in the metabolism of fats.
2. Is necessary in the storage of glycogen by liver and muscle cells.
3. Actively inhibits the formation of glucose from fats and protein.

Deficiency of insulin in man results in the condition known as *diabetes mellitus*. This condition was described by Auretaeus in the first century A.D. as a siphoning of flesh into urine; it is characterized by a high blood-glucose level (hyperglycemia), excess glucose in the urine (glucosuria), and diuresis, resulting in dehydration and constipation. Oxidation of carbohydrate is impaired; the resulting impaired oxidation of fats produces an accumulation of betahydroxybutyric acid, diacetic acid, and other fat breakdown products in the blood. The diabetic therefore suffers severe acidosis, depression, coma, and death if untreated.

Treatment of diabetes mellitus with insulin is replacement therapy, not a cure. Insulin prolongs life in the diabetic, and permits a fuller and happier life, but its use does not cure or prevent the disease. Insulin is especially valuable in preventing the complications of diabetes so frequently the cause of death: arteriosclerosis with hypertension, nephritis, superficial ulcers and infections, gangrene of the extremities, and gallstones. A fatty degeneration of the liver has been ascribed to the lack of a second pancreatic hormone, *lipocaic*, by some workers; others consider lipocaic identical with choline.

Conditions of hyperinsulinism are known, and may result from overdosage of insulin, underfeeding, tumors of the pancreas, or certain pituitary or adrenal disturbances. Outstanding symptoms are fatigue, hunger, marked sweating, and convulsions.

In the management of diabetes mellitus due to insulin deficiency, an adequate diet is determined, and the amount and spacing of insulin dosage is established to keep the patient symptom-free and free from glucosuria. One U. S. P. unit of insulin is capable of causing the metabolism of approximately 1.5 grams of glucose. Overdosage of insulin is applied to the development of convulsive shock in treating schizophrenic states.

Insulin is a protein, with a molecular weight of about 35,000. It was crystallized in 1926 by the addition of traces of zinc, and crystals of zinc insulin form the Reference Standard of the U. S. P. Potency is determined by comparing the hypoglycemic actions of unknown and Reference Standard insulins in selected rabbits by the official procedure. One U. S. P. unit of insulin activity is equal to the activity of the amount of Reference Standard Zinc Insulin Crystals stated on the label of the official Reference Standard. The potency of this Reference Standard ranges from 22 to 26 such units per milligram.

The iso-electric point of zinc insulin is at 5.1 to 5.3. Thus, it is soluble at the alkaline pH of tissue fluids, and is rapidly absorbed from subcutaneous injection sites. Insulin is digested by proteolytic enzymes, hence is ineffective when given orally.

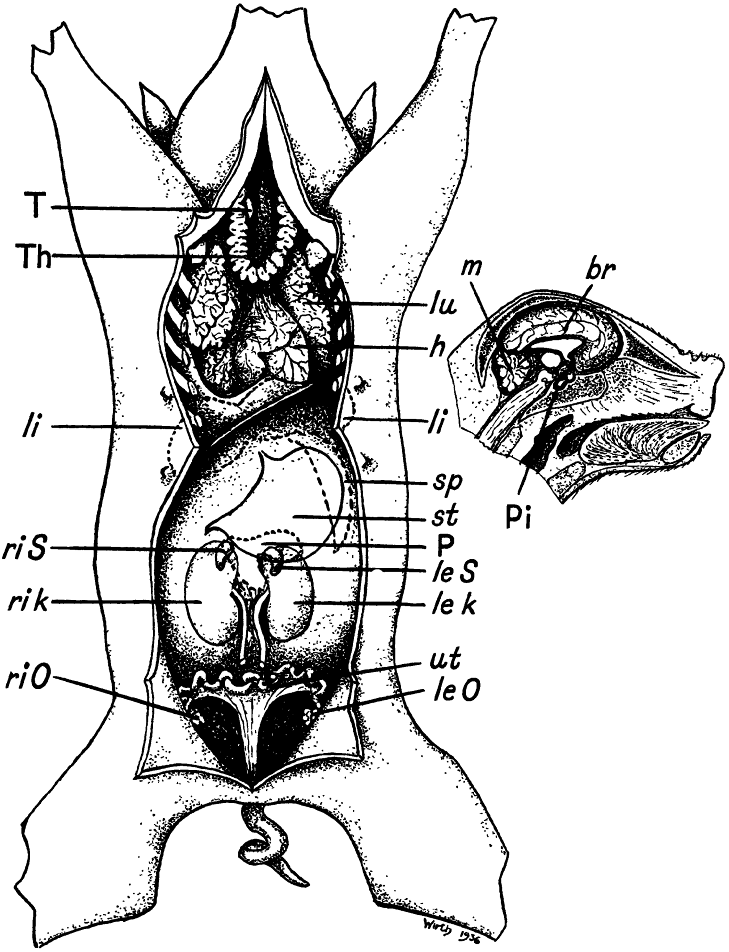


FIG. 370.—Diagrammatic sketches of the hog illustrating the location of the principal endocrine glands: *T*, thyroid; *Th*, thymus; *ri S*, right suprarenal gland; *le S*, left suprarenal gland; *ri O*, right ovary; *le O*, left ovary and *Pi*, pituitary. Other organs shown are: liver (*li*) (in outline); stomach (*st*) (in outline); spleen (*sp*) (in outline); right kidney (*ri k*); left kidney (*le k*); pancreas (*P*) (in outline); uterus (*ut*); brain (*br*) and medulla (*m*). The authors wish to acknowledge their thanks to Wilson & Co. of Chicago who made possible the dissection of the hog from which these sketches, as well as those for Fig. 371 were made. (Drawing by Wirth.)

Insulin Injection (U. S. P. 1942 to date) is an acidified solution of the active principle of the pancreas which affects the metabolism of glucose. It is described and standardized in the Pharmacopœia.

Insulin Injection provides rapid action by subcutaneous injection, with peak of action at two to four hours, and some effect over ten to twelve hours.

Protamine Zinc-insulin Injection (U. S. P. 1947 to date) is a suspension, in a buffered water medium, of insulin modified by the addition of zinc chloride and protamine. The protamine is prepared from the sperm or from the mature testes of fish belonging to the genera *Oncorhynchus, Suckley, Salmo* or *Trutta.*

Protamines are basic proteins—they combine with insulin to form protamine-insulin salts, stabilized by a trace of zinc. This complex has an iso-electric point of approximately 7.3—it is buffered to this point, and dispensed in a smooth suspension. When injected subcutaneously, it is insoluble at the pH of tissue fluids, and is therefore slowly absorbed to provide a prolonged action. Peak of action occurs at twelve to twenty-four hours, with some effect manifest over twenty-eight to thirty hours.

Modified Insulin (Unofficial).—This form is made by mixing the regular insulin solution with a suspension of protamine-zinc insulin, to provide in a single injection both immediate and prolonged control.

Globin Insulin With Zinc (N. N. R).—This product resembles Protamine-zinc Insulin Injection, and affords an action intermediate in onset and duration between that of regular insulin and of protamine zinc insulin. It is marketed in solution, but is insoluble at the pH of tissue fluids and is therefore slowed in its absorption. Maximum effect occurs at eight to twelve hours. A similar Histone-insulin with Zinc has not as yet achieved recognition.

Preparations of insulin are marketed in multiple-dose ampuls of varying unitage. Package color of commercial preparations varies with unit value, and the corresponding colors are listed in the current N. N. R.

Pituitary Body (Cerebral Hypophysis)

The human pituitary body is situated in a small cavity in the sphenoid bone at the base of the skull, and is attached to the base of the brain by a short stalk; it weighs about 0.5 gm. Galen considered it a strainer for spinal fluid, and Vesalius later thought it to be the source of mucus, lubricating the nasopharynx. Pituitary is from *pituita*—Latin for slime, or mucus. Modern information on pituitary function has been acquired within the past thirty to forty years.

The pituitary body is in reality two glands, by origin and function:

1. The anterior lobe is ectodermal in origin—derived from an outpouching from the primitive pharynx.
2. The posterior lobe is neural in origin—derived from an outpouching of the base of the brain.

A. **Posterior Lobe.**—Considerable uncertainty remains concerning the physiologic function and necessity of this part of the pituitary body. Extracts of posterior pituitary lobe exhibit the following effects in experimental animals and in man:

1. A pressor effect, due to arteriolar and capillary vasoconstriction;
2. Direct stimulation of smooth muscle, seen in the intact animal, or in preparations of isolated muscles;
3. An antidiuretic action, effected by increasing the tubular resorption of water in the kidney;
4. Metabolic effects, manifest in a lowered metabolic rate, and an antagonism to insulin.

These effects are all present in commercial preparations of the posterior pituitary lobe. Such preparations in therapeutic application have the disadvantage of unwanted side effects which may interdict their use. Fractionation of such extracts has produced two relatively pure hormonal preparations or fractions:

1. Pitocin (Oxytocin, Alphahypophamine) is the uterine-stimulating fraction, relatively free from action on other smooth muscle. It is especially active on the pregnant uterus, sensitized by estrogen.
2. Pitressin (Vasopressin, Betahypophamine). This fraction directly stimulates vascular, intestinal, and respiratory smooth muscle, and contains the antidiuretic principle.

The metabolic effects described above are present in both the pitocin and the pitressin fractions.

Official preparations of posterior pituitary are assayed for oxytocic activity on the isolated uterus of the virgin guinea-pig, in direct comparison with the Reference Standard Posterior Pituitary Powder of the Pharmacopœia. One U. S. P. unit of oxytocic activity is represented by 0.5 mg. of this Reference Standard by official assay. Pressor and antidiuretic activities in individual lots of posterior pituitary are not assayed, but tend to parallel oxytocic activity.

Pending final elucidation of posterior pituitary function, the following activities seem consistent with our present knowledge:

1. Some influence in the onset of labor at the termination of pregnancy; probably involving stimulus to a uterus sensitized by estrogen.
2. Some influence in the control of water balance by regulating the renal threshold for water.

No clinical conditions have yet been associated with hyperfunction of posterior pituitary. A deficiency state is seen only in the condition of *diabetes insipidus* which follows a deficiency of the antidiuretic principle.

Diabetes insipidus (literally an outpouring of tasteless urine) is characterized by a failure of renal resorption of water—there is a tremendous diuresis, with associated tremendous thirst and water intake. This condition must not be confused with the diabetes mellitus of insulin deficiency.

Preparations of posterior pituitary find therapeutic application as follows:

1. Replacement therapy in the management of diabetes insipidus.
2. Pharmacologic actions:
   (*a*) Stimulation to the postpartum uterus to lessen hemorrhage.

(*b*) Stimulation to depressed intestinal tonus, as may be seen following abdominal surgery.

Pitocin is generally preferred for the effects of posterior pituitary on the uterus, since its use avoids side-effects on the gut and circulation. Ergonovine is replacing some of the use of pituitary in the prevention of postpartum hemorrhage.

Whole Pituitary (N. F. 1936 to date).—The dried, partially defatted and powdered pituitary gland of cattle, sheep, or swine.

Posterior Pituitary (U. S. P. 1916 to date).—The cleaned, dried, and powdered posterior lobe from the pituitary body of domesticated food animals. By official assay, 1 mg. of this powder represents the activity of not less than 1 U. S. P. posterior pituitary unit.

These preparations, intended for oral therapy, are considered unreliable, inasmuch as the active principles are protein-like in character and are inactivated in the gastro-intestinal tract.

Posterior Pituitary Injection (U. S. P. 1916 to date) (Pituitrin).—A sterile, aqueous, injectable solution of the active principles of fresh posterior pituitary lobes from domesticated food animals.

This preparation represents the total activity of posterior pituitary. It is biologically standardized as described in the Pharmacopœia so that 1 cc. is equivalent to 10 U. S. P. units of oxytocic activity. In spite of the danger of undesirable side-effects on the gut, blood-pressure, the coronary arteries and the bronchioles, this preparation is frequently used in obstetrics for its oxytocic action.

Ampuls Pitressin (N. N. R.).—An aqueous solution of the pressor and antidiuretic principles of posterior pituitary (Betahypophamine). This preparation is unofficially standardized so that 1 cc. has a pressor activity equal to that exerted by 10 mg. of the U. S. P. Reference Posterior Pituitary Powder. This is twice the pressor activity of the official Posterior Pituitary Injection. Ampuls of Pitressin afford less than one unit of oxytocic activity per cubic centimeter.

Pitressin Tannate in Oil (N. N. R.).—A suspension of a tannate of the pressor and antidiuretic principles of posterior pituitary in a vegetable oil. This preparation is unofficially standardized to represent 5 pressor units per cubic centimeter—the pressor activity of 2.5 mg. of U. S. P. Reference Standard Posterior Pituitary Powder. It is particularly recommended in the maintenance treatment of diabetes insipidus. Intramuscular injections of 0.3 to 1 cc. at intervals of thirty-six to forty-eight hours provide adequate relief in the usual cases, due to slow, prolonged absorption from the oil vehicle.

Ampuls of Pitocin (N. N. R.).—An aqueous solution of the oxytocic principles of posterior pituitary (Alphahypophamine). One cubic centimeter represents the activity of 10 U. S. P. oxytocic units, with not more than one-half pressor unit.

B. **Anterior Lobe.**—This part of the pituitary body exerts a profound influence in the growth and development of the body and of its sex characters, both by direct hormonal activity, and through its stimulating actions on the other endocrine glands. A bit fancifully, anterior pituitary has been referred to as the "master-gland;" the "conductor of the endocrine symphony." As many as 18 functions have been ascribed to it. Of these, many are disputed, and many may be duplications. There is general agreement on the presence of:

1. One or more growth hormones. None of these has been isolated as yet. Overactivity of this part of anterior pituitary function during the growing period produces *giantism;* in the adult the picture is that of *acromegaly.* Hypofunction of the growth-stimulating activity during the growing period produces the *pituitary dwarf*—in the adult, such deficiency often results in an increased delicacy of structure referred to as *acromicria.*

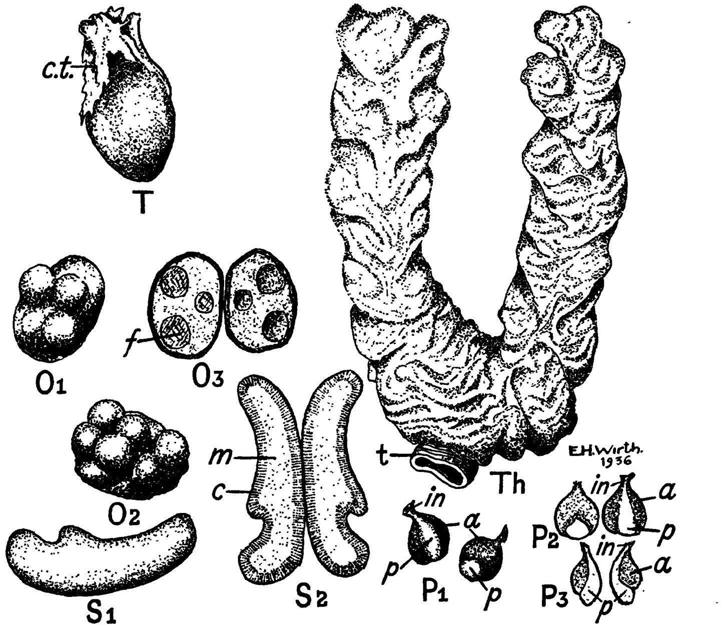


FIG. 371.—Endocrine glands of the hog: *T*, a lobe of the thyroid (a gland consisting of two lobes connected by an isthmus) showing at the upper end attached connective tissue (*c.t.*); *Th*, thymus with a portion of the trachea (*t*) attached; O_1, ovary from a young hog; O_2, ovary from a mature hog; O_3, ovary, cut longitudinally, showing the follicles (*f*); S_1, suprarenal gland; S_2, suprarenal, cut longitudinally, showing medulla (*m*) and cortex (*c*); P_1, pituitary gland showing lower side (at the left), and upper side (right); P_2, pituitary gland cut medianly more on the posterior side, P_3, pituitary gland cut dorsiventrally; *p*, posterior lobe; *a*, anterior lobe, *in*, infundibulum. The sketches are one-half natural size. (Drawings by Wirth.)

2. At least two gonadotropic activities:
   (*a*) The follicle-stimulating action, necessary to the ripening of the ovarian follicles, and to the maturation of the seminiferous tubules of the testes.
   (*b*) The luteinizing action, essential to the development and maintenance of the corpus luteum in the ovary, and apparently active in developing the gonadal cells of the testes.

In addition to these, hormones which have thyrotropic, lactogenic, diabetogenic, ketogenic, adrenotropic, and parathyrotropic activities are thought to be present. Obviously, primary disturbances in the functioning of anterior pituitary may result in widespread endocrine involvement and generalized secondary disturbances in growth, metabolism and development.

In spite of this tremendous physiologic importance, no preparations of anterior lobe have been accepted for inclusion in the Pharmacopœia or in N. N. R. This seeming contradiction is due to the present inability to isolate pure hormonal fractions from anterior pituitary. Side reactions of far-reaching significance are thus a source of danger in any preparation of this lobe. Unofficial preparations of growth hormone have been used with some success in pituitary dwarfism, but there is the attending risk of producing hyperthyroidism and sexual precocity due to the contaminating presence of thyrotropic and gonadotropic substances in commercial preparations.

Anterior Pituitary (N. F. 1936 to date).—The dried, partly defatted and powdered anterior lobe of the pituitary body of cattle, sheep or swine.

Intended for oral administration, this preparation is not reliable, and its use cannot be considered rational, since the contained hormones are readily destroyed in the gastro-intestinal tract, and since it contains an undetermined mixture of the various activities present in the total anterior lobe.

C. **Chorionic Gonadotropins** (Placental).—The blood serum of pregnant women contains a substance, elaborated by the placenta and excreted into the urine, which is similar in action to the gonadotropic action of anterior pituitary. This activity in pregnancy urines was first ascribed to substances elaborated by anterior pituitary—later, it was referred to as Prolan, or the Anterior-Pituitary-Like substance (A. P. L.), and recognized as originating in the placenta. The active substance is a water-soluble glycoprotein.

Chorionic Gonadotropin, Follutein or Korotrin, N. N. R. is the water-soluble gonadotropic substance obtained from the urine of pregnant women. It is a glycoprotein containing about 12 per cent of galactose. It is biologically standardized for gonadotropic activity in rats and mice. One international unit is that activity of 0.1 mg. of a standard powder prepared from a number of lots of human pregnancy urine. Since the material is of limited stability in solution, it is marketed in ampuls of dry powder, accompanied by ampuls of injection water.

It should be noted that chorionic gonadotropin is not truly gonadotropic in primates or human females. Follicle-stimulating and luteinizing actions are manifest in rats and mice; in the human female, follicular degeneration rather than stimulation is the usual result. Hence, Chorionic Gonadotropin is not intended for use in the human female. Its principal application is in the male, to encourage the descent of the testes into the scrotum in *cryptorchidism.* In such use, care in observation is necessary to avoid male sexual precocity.

Presence of chorionic gonadotropins in human pregnancy urines serves as the basis for the more frequently used laboratory tests for pregnancy, particularly the Aschheim-Zondek test, and the Friedman modification of this test. These tests are positive in pregnancy, and in certain tumors and other pathologic states of the uterus.

THE PARATHYROIDS

The parathyroid glands in man are usually four in number, oval, 5 to 6 mm. in length, and situated upon or imbedded in the dorsal surface of the thyroid gland. They develop and function independently of thyroid tissue. For a number of years after their discovery by Sandstrom in 1880, the parathyroids were considered to be remnants of embryonic thyroid tissue.

Parathyroid glands exert a hormonal control over calcium and phosphorus metabolism, in a manner not yet fully understood. Removal of, or deficiency of this function results in a fall in the serum calcium level, with an accompanying rise in serum inorganic phosphate.

Acute deficiency results in *tetany* when the level of serum calcium falls from normal (10 to 11 mg. per cent) to around 6 to 7 mg. per cent. Fibrillary muscular twitching progresses to the convulsive state, culminating in death by tetanic spasm of the larynx and the muscles of respiration.

Parathyroid hyperfunction produces a condition known as von Recklinghausen's disease, characterized by bone pain, marked elevation of serum calcium with fall in serum phosphate, cystic rarefaction of bones with spontaneous fracture and deformity. The calcium removed from bone is excreted in the urine. A similar picture may result from overdosage with extracts of parathyroid gland. In either case, renal stones and calcification of soft tissues occur.

Parathyroid function is correlated with the metabolic activity of vitamin D, which increases intestinal absorption of calcium, and favors its deposition in bone. There is some evidence that parathyroid influence regulates primarily the urinary excretion of phosphate, with compensatory changes in the serum calcium level; on the basis of other evidence, the mobilization of calcium is the primary action exerted by parathyroid activity.

The active principle (parathormone, paroidin) of parathyroid gland has not been isolated. It is evidently protein in nature, inactivated in the gastro-intestinal tract, and must therefore be given parenterally. Following injection, the blood calcium level rises in about four hours, reaching a maximum in about sixteen hours, and returning to normal in twenty-four to thirty-six hours. Hence, one dose daily is usually sufficient.

Parathyroid Injection (U. S. P. 1936 to date) is a sterile solution in water for injection of the water-soluble principle or principles of the parathyroid glands which have the property of relieving the symptom of parathyroid tetany and of increasing the calcium content of the blood serum in man and other animals. It is obtained from the fresh parathyroid glands of healthy domesticated animals used for food by man, the animal source of each preparation being stated. The parathyroid glands must be removed from the animals immediately after slaughtering, and then extracted at once, or kept frozen until extracted. The glands are freed from gross fat and connective tissue, ground, extracted and the extract purified to make it suitable for parenteral injection. The extract is then adjusted to the proper potency. This preparation is biologically standardized on its action in raising the serum calcium level in dogs, and its potency is adjusted to 100 U. S. P. units per cc. One U. S. P. unit of activity is 1/100th of the amount necessary to raise the serum calcium of an assay dog by 1 mg. per cent in sixteen to eighteen hours after subcutaneous injection as described in the official assay.

Parathyroid Injection is of particular value in controlling the tetany of acute parathyroid deficiency, and in replacement maintenance following surgical removal of the parathyroid glands. Repeated or prolonged administration may establish a complete tolerance with abolition of therapeutic effect. To avoid this, dihydrotachysterol may frequently be substituted; this preparation may be given orally. Adequate intake of calcium, phosphate, and vitamin D (calciferol) must be assured.

Thyroid Gland

The thyroid gland in man consists of two lobes, lateral and inferior to the anterior aspect of the larynx, and connected across the larynx by an isthmus to produce a "U" shaped structure averaging 30 grams in weight. Galen vaguely described the thyroid in the second century, but its identity as a ductless gland was first described by Holler in 1776. Interestingly enough, Roger of Palermo used sponges and seaweed, high in iodine content, in the treatment of goiter (thyroid enlargement) in the twelfth century.

Thyroid gland functions to mobilize dietary iodine, converting it to an organic compound which is capable of accelerating metabolic processes, and is necessary to the development and function of all body cells. The true thyroid hormone is presumed to be thyroglobulin, though the amino acid thyroxin exerts essentially the activity of the gland. The adult human body contains about 14 mg. of thyroxin, and this is maintained by the balanced use and production of about 0.33 mg. daily.

The following deficiency states may be described:

1. Simple iodine deficiency results in *simple goiter*—an enlargement of the gland considered compensatory to the lack of building material for thyroid hormone.

2. Deficiency of hormone produces varying degrees of:

(*a*) *Cretinism* in the infant, characterized by retarded and abnormal growth, arrested sexual development, mental deficiency, a thickened, dry skin, thickening of the tongue, coarsening of the features, and a fall in the metabolic rate.

(*b*) *Myxedema* in the adult, characterized by general lethargy;

retarded mental processes; increased body fat; susceptibility to cold and fatigue; cardiac dilatation; dry, thickened skin; and a coarsening of the features with a thickened, protruding tongue.

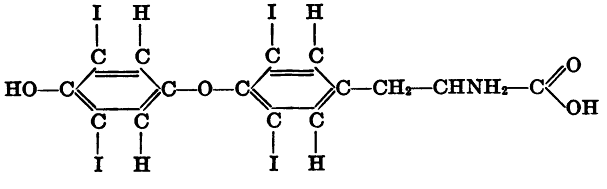
Thyroid hyperactivity results in *thyrotoxicosis*, characterized by increased heart rate, blood-pressure, nervous excitability, and metabolic rate; muscular weakness with tremor; loss of body weight and fat; and an increased tolerance to cold with intolerance of heat. When accompanied by protrusion of the eyeballs (exophthalmos) the condition is known as exophthalmic goiter (Graves' or Basedow's disease). The course is marked by occasional crises or "storms," which may result in abrupt death. These symptoms of thyroid hyperactivity may result from overdosage of thyroid preparations, as frequently occurred in the irrational use of obesity "cures" containing thyroid. Treatment of organic hyperthyroidism is principally surgical, aided by iodine and by the use of thiourea, thiouracil, and derivatives of these. There is recent evidence that these latter agents may supplant surgery in selected cases.

Preparations of thyroid gland are of value in:

1. Specific replacement therapy in myxedema, or in the prevention of myxedema following surgical removal of the thyroid gland.
2. Replacement therapy in cretinism. Here early diagnosis and treatment are essential in avoiding irreversible bodily and mental retardations.

Thyroid (U. S. P. 1905 to date) is the cleaned, dried, and powdered thyroid gland previously deprived of connective tissue and fat. It is obtained from domesticated animals that are used for food by man. Thyroid contains not less than 0.17 per cent and not more than 0.23 per cent of iodine in thyroid combination, and must be free from iodine in inorganic or any other form of combination other than that peculiar to the thyroid gland. A desiccated thyroid of higher iodine content may be brought to this standard by admixture with a desiccated thyroid of a lower iodine content, or with lactose, sodium chloride, starch or sucrose. This material is effective by oral administration, and when so given, this preparation is the choice preferred in thyroid therapy.

Thyroxin (U. S. P. 1926 to date) is the active principle isolated from the thyroid gland, or prepared synthetically, and contains not less than 64 per cent of integrally combined iodine. One milligram increases the adult basal metabolic rate by approximately 2 to 2.5 per cent. Synthesized by Harrington and Barger in 1927, thyroxin has the following structure:



Thyroxin is poorly and irregularly absorbed from the intestinal tract, and is therefore not satisfactory for oral administration. It may be given intravenously, but such use requires careful alkalinization to effect solution, is relatively expensive, and offers no advantage over oral thyroid in the usual case. Thyroxin is seldom employed at the present time.

The effect of a single dose of thyroid orally, or of thyroxin orally or intravenously, is not manifest for some twenty-four to forty-eight hours; reaches a maximum in eight to ten days, and decreases slowly over a period of several weeks. Hence, accumulation may occur, and dosage schedules must be adjusted individually to the needs of the patient.

Adrenal Glands

The adrenals (suprarenals) in man comprise a pair of small glands, one situated over the superior medial aspect of each kidney. Each average gland measures 5 x 25 x 50 mm.; together the adrenals weigh 4 to 18 grams.

The adrenals were first described by Eustachius in the sixteenth century, and were long supposed to function in the inhibition of fetal urination, and in the prevention of renal stones in the adult. Knowledge of adrenal function began with Addison in 1849, and is as yet far from being completed.

Each adrenal consists embryologically, histologically and functionally of two distinct glandular entities, grossly combined into one organ:

1. The adrenal medulla is composed of cells which migrated out from the embryonic neural crest, and are analogous to the peripheral sympathetic neurons of the autonomic nervous system. Its hormone, epinephrine, is identical with or closely approximates the sympathetic neurohormone, sympathin. Adrenal medulla functions as a sympathetic postganglionic structure.
2. Adrenal cortex is composed of cells arising behind the primitive sex cells on the genital ridge of the embryo. Its functions in close correlation with gonadal function, and its hormones are steroids, similar in structure to the sex hormones of ovary and testis.

A. **Adrenal Medulla.**—Adrenal medulla is not essential for life, and no diseases of deficiency are known. Therapeutic use of the hormone, epinephrine, is based upon the pharmacology of the sympathicomimetic amines, rather than upon the principle of replacement. Epinephrine is a vasoconstrictor and vasopressor, acting in general as a sympathicomimetic agent of rapid onset but brief duration of action. It is capable of inhibiting isolated intestinal strips in dilutions as high as one to four million. Oral administration of epinephrine is ineffective, due to inactivation in the stomach.

Suprarenal, Desiccated Suprarenal or Dried Adrenal Substance (U. S. P. 1905 to 1926; N. F. 1936 to date) is the dried, partially defatted and powdered suprarenal gland of cattle, sheep or swine. Suprarenal is derived from sound, clean, and entire glands that are freed from external connective tissue and external fat. It yields not less than 0.8 per cent of natural epinephrine of glandular origin and is free from diluents or preservatives. One part of suprarenal represents approximately 6 parts by weight of the fresh glands. If suprarenal is dried by heat, it must be dried in a vacuum, the temperature of the drying material not exceeding 60° C. The preparation is intended for oral use, but is considered archaic by most physicians.

Epinephrine (U. S. P. 1926 to date) (**Suprarenalin, Adrenalin**). A levorotatory alkaloid isolated from adrenal medulla, or prepared synthetically. Dextrorotatory epinephrine is almost completely inactive, and optically inactive mixtures have about half the activity of natural epinephrine. Epinephrine alkaloid is official for use in the preparation of solutions and other administration forms.

Epinephrine Solution or Epinephrine Hydrochloride Solution (U. S. P. 1926 to date) is a solution of epinephrine in distilled water prepared with the aid of hydrochloric acid. It has a potency equivalent to a solution containing 1 gm. of U. S. P. Epinephrine Reference Standard in each 1000 cc. It is standardized on the basis of its pressor effect in prepared dogs, by direct comparison with Reference Standard Epinephrine.

Epinephrine Injection or Epinephrine' Hydrochloride Injection (U. S. P. 1942 to date) is a sterile solution of epinephrine in water for injection prepared with the aid of hydrochloric acid. The injection is intended for systemic or local use by subcutaneous or intramuscular injection.

Epinephrine Inhalation (U. S. P. 1947 to date) is a solution of epinephrine in distilled water prepared with the aid of hydrochloric acid. It has a potency equivalent to a solution containing 1 gm. of U. S. P. Epinephrine Reference Standard in each 100 cc. The solution is intended only for topical application to the bronchial mucous membrane in the form of a finely vaporized spray. It affords relief in bronchial asthma with a minimum of systemic side effects. It must not be confused with the weaker solutions or injections previously described.

Suspension of Epinephrine in Oil (N. N. R.).—A 1:500 suspension of epinephrine base in vegetable oil, suitable for intramuscular injection. This preparation is slowly absorbed from the intramuscular depot, and affords a modified, prolonged epinephrine action from a single injection. It affords prolonged relief in bronchial asthma, hay-fever, urticaria, and other allergic manifestations.

B. **Adrenal Cortex.**—The adrenal cortex is essential to life—removal of about 85 per cent of cortical tissue results fatally in a few days. In animals so treated, life may be maintained by the administration of extracts or hormones of the adrenal cortex.

Cortical deficiency in animals is marked by a loss of appetite and weight; vomiting and diarrhea; weakness; and a fall in temperature, metabolism, and blood-pressure. There is a loss of blood fluid, with resulting concentration of blood, a fall in serum sodium with a rise in serum glucose and potassium. Kidney damage is frequently present. These developments can be prevented or restored to normal by the administration of cortical extracts, and frequently by the simple use of a high sodium, low potassium intake.

The human counterpart of this deficiency picture is seen in the clinical development of *Addison's disease,* due usually to tuberculosis or tumor of the adrenal cortex. Associated with this disease, there is degeneration of the gonads, a marked increase in capillary permeability, and an increased sensitivity to insulin. Sodium loss with potassium retention may be the outstanding condition of the disease. If untreated, Addison's disease terminates fatally in one to three years, due usually to hypoglycemia, dehydration, nutritional disturbances or secondary infection.

Excessive adrenal cortical activity, as in tumors or due to the presence of accessory cortical tissue, result in profound growth abnormalities, especially seen in the external genitalia, and in the secondary sex characteristics. In young children, there is precocious sexual development and desire, with obesity or unusual muscular development. In adult females, there is commonly the development of virilism, associated with a masculine appearance, often with homosexuality. The bearded lady of the circus is frequently of this category. Treatment of cortical overactivity is principally surgical.

Some twenty or more crystalline steroids have been isolated from cortical extracts. These exhibit in some degree the action of adrenal cortex. Some in addition manifest estrogenic, androgenic, and progesterone-like activity, further indicating the close relationship between adrenal cortex and the gonads.

Corticosterone was crystallized from cortical extracts by Reichstein in 1936. It has not been synthesized, and the natural steroid is prohibitively expensive. It is present in crude cortical extracts, and functions principally in opposing insulin to restore normal blood sugar levels and glycogen storage.

Preparations of adrenal cortex are used primarily as replacement therapy in Addison's disease, and in surgical adrenal cortex deficiency. This therapy, especially using cortical extracts, is markedly improved by the use of high sodium, low potassium diet regulations. Dosage must be established in the individual, based upon need. Attempts to use cortical extracts in the management of surgical shock, based upon their action in reducing capillary permeability, are as yet experimental.

Adrenal Cortex Extract (N. N. R.) is an extract of adrenal glands, from domesticated animals used as food in man, containing the cortical steroids essential for the maintenance of life in adrenalectomized animals. Only traces of epinephrine are present.

Desoxycorticosterone Acetate (U. S. P. 1947 to date).—This steroid was identified in cortical extracts by Reichstein and his associates in 1938, and later was synthesized from stigmasterol. Material in present use is the synthetic product, due to the greater cost of the natural hormone.

Cortical extracts are effective when given orally, but better and more uniform results follow the intramuscular injection of desoxycorticosterone dissolved in sterile vegetable oil. Pellets have been successfully implanted in the subcutaneous tissues for even more prolonged action. Desoxycorticosterone is relatively ineffective orally.

Desoxycorticosterone functions primarily in restoring a balance of sodium and potassium in body fluids, and in restoring kidney function, in cortical deficiency. Death from hypoglycemia may occur in Addison's disease treated with desoxycorticosterone alone; such cases require the use of cortical extracts.

The Gonads

The ovaries and testes are exocrine (ova, sperm) as well as endocrine (hormonal) in function. They develop under the influence of anterior pituitary hormones, particularly:

1. The follicle-stimulating hormone (FSH) leads to the development of the ovarian follicles, to their formation of ova and of estrogen, and to the development of the testes and the maturation of the spermatozoa.
2. The luteinizing harmone (LH) is necessary to the development of the corpora lutea in the ovarian follicles after ovulation, to the formation of progesterone by the corpora lutea, and to the production of androgen in the matured testis.

Androgens (male hormones) and estrogens (female follicular hormones) act to:

1. Develop and maintain the secondary characters of sex.
2. Depress anterior pituitary function, leading in turn to the depression of the testis or the ovary.

Progesterone (corpus luteum hormone) similarly depresses anterior pituitary function, and presents a mixed antagonism-synergism with estrogenic activity, as will be indicated below.

Gonadal hyperactivity, or excessive therapy may thus result in a picture of precocious or excessive sexual development, together with the generalized effects of anterior pituitary depression. Gonadal hypoactivity, as in the natural menopause, or following surgical removal of the gonads, results in a mixed picture of sexual regression, and enhanced anterior pituitary activity, with psychic disturbance, and the involvement of other endocrine glands, particularly the thyroid.

A. **The Testes.**—Following castration in the male, the sex organs atrophy, and sexual desire and activity are diminished. These functions are restored by the administration of testes hormone. Hypogonadism (enuchoidism) is a failure of adequate development of the testes, due to pituitary disorder, infection, or other disease. Therapy of this condition is still in the experimental stages.

Hypergonadism is most frequently seen in young males, due to testis tumors, and resulting in precocious development of sex organs and male characteristics. Therapy is usually surgical.

Testosterone Propionate (U. S. P. 1947 to date).—The active male hormone, isolated from bull's testis, or synthesized from cholesterol. Testosterone is believed to be the true testis hormone, although it has been identified only in the bull's testis (David, 1935). It was synthesized by Ruzicka from cholesterol in 1936. Androsterone and dehydro-iso-androsterone are urinary excretion products, relatively inactive in man.

Testosterone given orally is rapidly absorbed and excreted. Action is further shortened by partial destruction, probably in the liver. Better therapeutic effect is achieved by measures designed to delay the absorption, excretion, or destruction of the testosterone. Testosterone Propionate is given by intramuscular injection in doses of 25 mg.

Methyltestosterone (U. S. P. 1947 to date) given orally or sublingually, in doses of 10 mg. or 5 mg., respectively, provides prolonged activity due to a decreased rate of destruction.

Similarly, unofficial pellets of testosterone propionate have been successfully implanted under the skin. These may provide activity for a year or more; on the other hand, encapsulation in fibrous tissue may occur to render the implant valueless.

Testes hormone preparations have shown evidence of value in the replacement therapy of male castrates and enuchoid states, and in the treatment of certain female ovarian dysfunctions. Much of this therapy is still in the experimental stages. It must be remembered that testosterone is not an aphrodisiac, and that its use may produce the general effects of anterior pituitary depression. It may produce virilism in the female, and skin reactions similar to acne vulgaris rather frequently develop. Therapy with testosterone may be prohibitively expensive.

B. **The Ovary.**—The human ovaries are paired organs, one being situated on each lateral pelvic wall, in the posterior layer of the broad ligament, behind and below the lateral extremity of each Fallopian tube (oviduct). Each is about the size and shape of an unshelled almond, and weighs about 4 to 8 grams.

Ova develop within primitive ovarian follicles (Graafian follicles) under the influence of the follicle-stimulating hormone of anterior pituitary. Ovulation with the extrusion of one ovum from a ripened follicle normally occurs each month during the child-bearing period. If pregnancy is established, the ruptured follicle undergoes cellular change to become the corpus luteum, under the influence of the luteinizing hormone of anterior pituitary. The ovary elaborates two types of hormone:

1. Estrogens, elaborated in the developing Graafian follicle, and probably also in the placenta during pregnancy.
2. Progestins, elaborated by the corpus luteum, and, in the latter half of pregnancy, by the placenta.

I. **Estrogens.**—Deficiency in estrogenic activity is most frequently manifest in the normal menopause, or following surgical removal of the ovaries. Local changes in the tissues of the vagina and vulvæ may result from estrogenic deficiency of any cause.

The estrogens are necessary to:

1. Develop and maintain secondary female sex characters.
2. Develop and maintain the uterus and the vagina.
3. Aid in the presecretory development of the mammary glands.
4. Maintain the corpus luteum of pregnancy.

Estrogens act further to excite or sensitize the uterine muscle, and to depress the anterior pituitary function. Preparations of estrogenic substances are employed in the management of:

1. Symptoms of the natural or surgical menopause.
2. Local atrophic and degenerative changes in the adult vagina and vulva, resulting from estrogen deficiency.
3. Gonorrheal vaginitis in the young female child, by inducing an adult type of vaginal epithelium, resistant to the gonococcus.
4. Suppression of lactation in engorged, painful mammary glands, presumably by a direct action in the breast. Stilbestrol orally is most frequently employed for this purpose.
5. Prostatic cancer in the male, presumably by balancing an excessive persistence of androgen—the principle of "biochemical castration."

Ovary (N. F. 1936 to date) is the dried, undefatted, and powdered ovary of cattle, sheep or hogs. One part of Ovary represents approximately 6 parts of fresh glands.

Ovarian Residue (N. F. 1936 to date) is the dried, undefatted, and powdered ovary of cattle, sheep or hogs, from which the corpora lutea have been removed. One part of Ovarian Residue represents about 6 parts of fresh gland, without corpora lutea.

Intended for oral administration, in doses of about 0.3 gm., these preparations are of unknown potency and efficiency, and their use has been rendered more or less obsolete by the development of isolated and purified active principles and preparations.

Isolated or Purified Estrogens:

I. Crystalline estrogens of natural origin.
  - **Estradiol** (U. S. P. 1947 to date).
  - **Estradiol Benzoate** (U. S. P. 1942 to date).
  - **Estriol** (estratriene, theelol) (N. N. R.).
  - **Estrone** (theelin) (U. S. P. 1942 to date).

II. Crystallized Synthetic Estrogens.
  - **Diethylstilbestrol** (U. S. P. 1947 to date) (Stilbestrol).
  - **Benzestrol** (octofollin) (N. N. R.).
  - **Hexesterol** (N. N. R.).

III. Non-crystalline Estrogens.
  - **Amniotin** (N. N. R.).—This preparation is water-insoluble, and consists principally of estrone, extracted from pregnant mares' urine.
  - **Premarin** (N. N. R.).—This preparation is water-soluble, and consists principally of sodium estrone sulfate, extracted from pregnant mares' urine.

The natural ovarian hormones are steroids. Alpha-estradiol is believed to be the true ovarian hormone, although it has as yet been identified only in the sows' ovary. Beta-estradiol is virtually inactive. Estradiol, U. S. P. is alpha-estradiol, prepared by the reduction of estrone, and possessing some 6 times the potency of the latter.

Estrone and estriol are oxidation products of estradiol, recoverable from human pregnancy urine, follicular fluid, placenta, and from the urine of pregnancy mares. Crystalline synthetic estrogens are non-steroid derivatives of stilbene, and offer inexpensive, orally effective estrogenic activity.

Crystalline estrogens are prescribed in terms of weight, based on the individual need. The non-crystalline estrogen preparations are standardized unofficially on the uterus of the castrated female rat, one international unit representing the activity of 0.1 mg. of crystalline estrone. Other rat units vary widely and should be disregarded.

Estrogens may be administered orally, parenterally, or by inunction for systemic activity. Orally administered natural estrogens are destroyed in greater part, probably in the liver. Estriol is the best of this group for oral use—oral efficiency of estriol is about one-fifth that achieved by parenteral administration. Synthetic estrogens are cheaper, and more effective by the oral route than natural estrogen.

Given parenterally, about 90 per cent of natural estrogen is destroyed. This factor, in addition to rapid absorption, tends to diminish the efficiency and effective period of therapy. In the case of the crystalline synthetic estrogens, absorption is rapid, but destruction is slow, so that a more prolonged period of action is achieved. Side effects of nausea and vomiting are likewise enhanced.

Therapeutic efficiency is improved by:

1. Formation of esters, such as estradiol benzoate, and estradiol propionate. Esterification slows destruction and elimination, and thus prolongs the duration of effect following oral or parenteral administration.
2. Intramuscular injection of estrogen esters, dissolved or suspended in sterile vegetable oil to prolong action further by slowing absorption. Similarly, pellets of estrogen esters have been successfully implanted under the skin, and may be effective for months. Slowed absorption further lessens side-effects of nausea and vomiting.
3. Suppositories containing estrogenic substances provide local treatment of changes in the vagina or vulva, or treatment of gonorrheal vaginitis in female children, with a minimum of systemic effect.

The natural estrogens exhibit carcinogenic properties upon prolonged administration to animal strains having hereditary susceptibility to mammary cancer. There is a feeling that on this basis, estrogens should be contra-indicated in women who have a personal or family history of mammary or genital cancer. In this connection, it is interesting to note the recent experimental use of estrogens and of androgens in the treatment of certain cancers occurring in females.

II. **Corpus Luteum-progestin.**—The corpus luteum is essential to the maintenance of human pregnancy during the first half of the term. Its principal hormonal functions are:

1. Preparation of the uterine mucosa to receive the fertilized ovum.
2. A necessary rôle in the development of the maternal placenta.
3. Continuation of the development of the mammary glands, in preparation for the lactogenic action of anterior pituitary.
4. Suppression of ovulation for the duration of pregnancy.

5. Antagonizing the stimulating effect of estrogens on the uterine muscle, to produce a relaxation of the uterus.

Corpus Luteum (N. F. 1936 to date) is the dried, undefatted, and powdered corpus luteum from the ovary of cattle, sheep or swine. One part of corpus luteum is obtained from approximately 5 parts by weight of fresh corpus luteum.

The active hormone of the corpus luteum is believed to be progesterone, and this steroid has been synthesized from stigmasterol. It appears in pregnancy urine in an inert reduction derivative termed pregnandiol, which may be recovered and oxidized to progesterone.

Progesterone (U. S. P. 1947 to date).—This substance is ineffective when given orally, and is usually administered intramuscularly in oil solution, in doses of 5 mg.

Anhydro-hydroxyprogesterone (U. S. P. 1947 to date).—This derivative of progesterone exhibits progestin activity when given orally in doses of 10 mg.

Therapeutic usage of these progestins is not well established, and no preparations of corpus luteum or its hormones have been accepted for inclusion in N. N. R. (1946). Extracts of corpus luteum as well as the crystalline hormones have been extensively employed in the treatment of habitual abortion, in the relief of pain after childbirth, and in the relief of cramping pain associated with uterine overactivity during the menstrual period. These actions probably depend upon a relaxation of uterine muscle.

LIVER-STOMACH

These organs serve an endocrine function in collaborating to produce one or more hormonal principles essential to adequate functioning of the erythropoietic bone marrow, and to other less clearly defined functions. The essential substance is referred to as the "anti-anemia principle" (A. A. P.), or the "erythrocyte-maturing factor" (E. M. F.).

Deficiency in the supply or utilization of this hormone leads to complex disturbances centering around a severe anemia, and characterized by one or more of the following:

(*a*) Hyperchromic, macrocytic anemia (Addisonian Pernicious Anemia). This condition was described by Combe in 1822, and more fully by Addison in 1849.

(*b*) Gastro-intestinal disturbances: Smoothing and inflammation of the tongue, digestion disturbances, and diarrhea, associated with lack of gastric hydrochloric acid.

(*c*) Nervous disturbances, involving particularly the spinal cord and the peripheral nerves.

(*d*) Bone marrow changes, with a cessation of erythrocyte maturation at the stage of abnormal megaloblasts.

In untreated cases, the disease progresses by repeated episodes of these changes, to a fatal termination. Adequate replacement therapy is available in oral or parenteral preparations containing the essential hormone, prepared from the stomachs or livers, or both, of domesticated food animals.

Under conditions of normal function, the elaboration of this essential hormone may be outlined as follows:

1. An adequate diet contains an unknown substance, designated as the "extrinsic factor"—associated with but apparently not a part of the B complex of vitamins.
2. Gastric and duodenal glands secrete a substance—the "intrinsic factor"—probably a proteolytic enzyme.
3. Interaction of these factors occurs in the small intestine.
4. This interaction product is carried to the liver, where the ultimate hormone is elaborated and stored, pending release to the bone marrow and other organs.

Pernicious anemia may result from defects at any point between the dietary intake and the utilization of the hormone in the bone marrow. The most common defects lie in an inadequate production of intrinsic factor, and in an inadequate absorption of the interaction product from the small intestine.

Minot and Murphy in 1926 showed that the daily oral ingestion of 200 to 400 grams of whole liver resulted in remission of pernicious anemia, and the maintenance of a normal erythrocyte and marrow picture. This whole liver must be ingested raw, or at most lightly cooked, since the active hormone is destroyed by more thorough cooking. Preparations at present in use are the result of improvements in the extraction of the hormone from the livers and stomachs of food animals.

Preparations of Liver, Stomach, or Liver-stomach, are bio-assayed for their activity in inducing remission in patients suffering from active pernicious anemia in relapse. Assignment of potency is made by the Anti-anemia Preparations Advisory Board of the U. S. Pharmacopœia, on the basis of data supplied by the manufacturer. One U. S. P. Anti-anemia Unit is the minimum amount of the material in question which must be given daily to produce an adequate hematopoietic response, as determined by this Advisory Board.

The amount of substance necessary to provide this adequate response by oral administration is about 30 to 40 times that required by intramuscular injection. Hence, labelled potencies are specified in "oral" or "injectable" units, depending upon the route to be used in administering the product so labelled.

I. **Liver Extracts.**—The active material present in liver extracts has the properties of a peptide, with a molecular weight of five to ten thousand. It is water-soluble, stable at 100° C., at pH 5, and is readily absorbed from the intestine or from intramuscular injection sites.

A. **Oral Liver Extracts.**—**Liver Extract** (U. S. P. 1936 to date) is a dry, brownish, somewhat hygroscopic powder, and contains that soluble thermostable fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons affected with pernicious anemia. The approximate anti-anemia potency of Liver Extract in pernicious anemia is expressed in U. S. P. Units (oral).

Liver Solution (U. S. P. 1936 to date) is a brownish liquid, and contains that soluble thermostable fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons affected with pernicious anemia. The approximate anti-anemia potency of Liver Solution in pernicious anemia is expressed in U. S. P. Units (oral).

Oral liver preparations are preferable to raw liver for therapy, but have given way largely to more purified parenteral preparations, or to oral Liver-stomach Concentrates. Oral Liver Extracts are relatively expensive, often unpleasant to the point of nauseating the patient, slow, and relatively uncertain in their action. In severe cases, particularly if complicated by nausea, vomiting, diarrhea, or established nervous system changes, oral therapy is frequently inadequate.

B. **Parenteral Liver Extracts.**—**Liver Injection** (U. S. P. 1947 to date) is a sterile solution in water for injection of that thermostable fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons affected with pernicious anemia. The approximate anti-anemia potency of Liver Injection upon intramuscular administration in pernicious anemia shall be expressed in U. S. P. Units (Injectable). Liver Injection contains not more than 15 U. S. P. Units (Injectable) in each cubic centimeter.

Parenteral Liver Extracts are protein-free, sterile, purified products, designed for intramuscular injection. Commercial preparations are available in a range of concentrations providing 1 to 15 injectable units per cubic centimeter; at the present time, no preparation will be assigned a potency value in excess of 15 units per cubic centimeter.

Preparations of the lower potency values are preferred by many—the bulk of injected material per unit is of course greater, but these preparations of lower potency are relatively crude, and contain appreciable quantities of vitamins and of other, poorly understood fractions believed to be present in whole liver. High potency preparations are preferred in specific therapy of pernicious anemia of severe degree, or in the presence of advanced nervous system disturbances.

Intramuscular injection is the preferred route for liver therapy, due to:

(*a*) More rapid utilization, permitting greater efficiency and more effective dosage.

(*b*) Greater convenience of administration. Patients may be taught to inject themselves, and maintenance may often be achieved on single weekly injections.

(*c*) Economy, due to more efficient utilization.

II. **Stomach Preparations.**—These consist of the dried, powdered, defatted stomach of the hog. They are intended for oral administration —no parenteral preparations of Stomach are available. These preparations contain the interaction product, resulting from the action of intrinsic factor from the mucosal glands upon the extrinsic factor contained in the muscular part of the stomach wall.

Powdered Stomach (U. S. P. 1936 to date) is the dried and powdered defatted wall of the stomach of the hog, *Sus scrofa* var. *domesticus*. It contains factors which increase the number of red blood corpuscles in the blood of persons affected with pernicious anemia. The activity is readily destroyed when the preparation is suspended in a hot liquid. The approximate anti-anemia potency of Powdered Stomach in pernicious anemia is expressed in U. S. P. Units (oral). **Ventriculin** N. N. R. is a similar preparation.

Powdered Stomach is more agreeable to taste than oral liver extracts, hence produces less nausea, and may thus be more dependable—otherwise, the disadvantages of Powdered Stomach in therapy are those outlined for oral liver preparations.

III. **Liver-Stomach Preparations.**—These are powders, prepared in general by digesting about 3 parts by weight of crude liver extract with one part of finely minced hog stomach mucosa. The active hormone present is supplied in part by the liver extract, and in part by the interaction between the extrinsic factor present in the liver extract with the intrinsic factor of the gastric mucosa. Digestion thus enhances the final anti-anemic potency to approximately ten times that of the reacting ingredients. Liver-Stomach is the most potent of the oral anti-anemia preparations; no parenteral preparations are available.

Liver with Stomach (U. S. P. 1947 to date) is a brownish powder resulting from mixing a concentrated water solution of mammalian liver with minced fresh hog stomach tissue. The fraction of liver employed is soluble in approximately 70 per cent alcohol, by volume, and insoluble in approximately 95 per cent alcohol by volume. After admixture and incubation, the product is dried under reduced pressure, and defatted. The approximate anti-anemia potency of Liver with Stomach in pernicious anemia is expressed in U. S. P. Units (oral). Extralin N. N. R. is a similar product.

Two general points must be considered in the therapeutic use of these anti-anemia preparations of liver and stomach:

1. Their use is replacement therapy—not curative. Relapses may be expected to follow cessation of therapy.
2. Pernicious anemia results from a specific deficiency, supplied by the specific anti-anemia factor. The popular addition of vitamins, iron and other factors to therapy is justified only upon the basis of an established need for them—they are of no specific value in pernicious anemia.

Recent experimental studies have indicated the value of folic acid in the treatment of macrocytic anemias. This substance is probably identical with "Vitamin Bc" or the "Lactobacillus casei factor" previously reported in crude liver extracts, yeast, animal muscle, and other sources. Synthetic folic acid (Pteroylglutamic Acid) has shown experimental promise in macrocytic anemias associated with sprue and related conditions. (See Vitamin B, p. 675.)

POWDERED DRUGS

A very appreciable amount of the traffic in crude drugs consists of drugs that have been reduced to a powder. Milling destroys practically all means of macroscopic identification, leaving as the only means of identifying the drug the microscopic characteristics of the tissue elements and cell contents, together with their reaction toward microchemical reagents and in a few cases their odor and taste.

Examination.—The powder to be examined should be so mixed as to insure a uniform sample. Before making a microscopic examination, especially in the case of coarsely comminuted material, it is desirable to mix a small quantity of the material with a little water contained in a watch crystal or small beaker and note such features as the following: (1) *If the particles sink or float.* In all genuine coffee, for instance, the particles rise to the surface, whereas in the substitutes and adulterants they sink. (2) *If the particles disintegrate.* Artificial products when made from exhausted powders or spurious substances, slowly disintegrate, leaving a fine sediment. (3) *The color of the solution.* A chelidonium powder, for instance, gives a golden-yellow solution, as do also many drugs containing berberine and allied principles. (4) *Behavior of the solution and particles toward alkalis or dilute hydrochloric acid.* Drugs containing hydroxymethyl-anthroquinone derivatives, as senna, rhubarb, aloe, frangula and cascara sagrada, are colored red with alkalis. The particles of ruellia give a distinct effervescence with hydrochloric acid, particularly if the mixture is slightly heated. The presence or absence of starch may be determined by heating the mixture, to which has been added a few drops of diluted hydrochloric acid, filtering and adding iodine to the filtrate when cool.

The odor of the mixture, particularly on warming, is of considerable value, as in the detection of belladonna in inula or of conium in anise. The odor is also of value in recognizing the specimen, as many drugs have a characteristic odor. The odor of a specimen is, however, sometimes misleading, as a number of substances not at all related may have a similar odor. The odor of elm bark, for instance, is possessed by other substances, such as fenugreek and wheat middlings, particularly if these substances are kept in closed vessels.

The fixed oil, which occurs in considerable quantity in many seeds, often interferes with their microscopic examination and in such cases it is necessary to remove it before making mounts of the material. This can be accomplished by treating the powder with chloroform, xylol, acetone, ether or other similar solvent. Alcohol, as a rule, is not a good solvent for these oils. The solvent may be added directly to the mount and the solution absorbed by means of filter paper.

In preparing a mount for microscopic examination the following method gives good results. Place 2 or 3 drops of the reagent or mounting medium on a clean slide. By means of a teasing needle, transfer a suitable quantity of the powder to the reagent, mixing it well with the liquid. Place the cover-glass, allowing one edge to touch the slide first, and by light pressure with the finger move the cover-slip in rotary motion to ensure an even distribution of the powder beneath it. Both the amount of powder and the amount of reagent to use must be learned by experience. A properly prepared mount will just fill the space between slide and cover-glass and will be but slightly opaque.

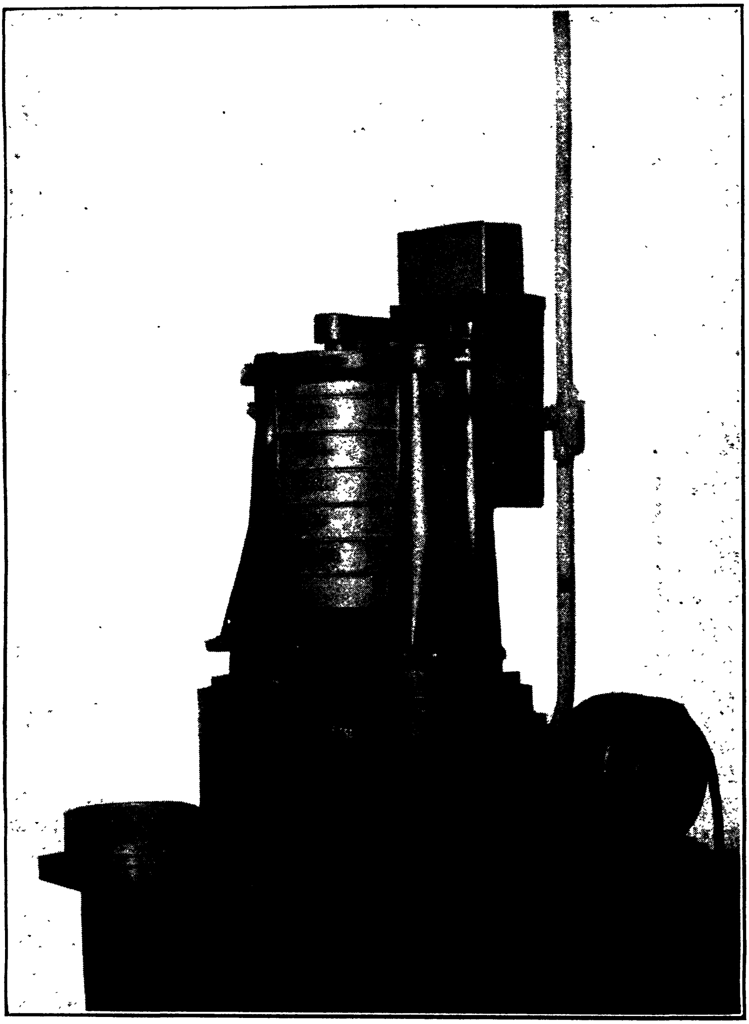


FIG. 372.—Ro-Tap Sieve Shaker. Drug Milling Laboratory, College of Pharmacy, University of Minnesota.

The proper reagent or mounting medium to be used depends upon the characteristic tissue element sought. Tracheal tissue, bast, wood fibers and sclerenchyma tissue generally give a red reaction with phloroglucin-hydrochloric acid. Chloral T.S. serves as a clearing agent and is not applicable to the study of starch grains, but is very useful in the study of mechanical tissues, hairs and calcium oxalate. The clearing action may be hastened by the application of heat before the cover-glass is placed. In using iodine solution for the identification of starch microscopically, care should be taken that the reagent is not too concentrated. A preferable way of performing this test is to mount the powder in water in the usual way. A drop of iodine solution is then placed on the slide at one side of the cover-glass and drawn under it by means of a piece of filter paper applied at the opposite side. The characteristic blue (not black) is noted when the reagent first comes in contact with the starch grains. Among other special reagent solutions are ammonio-ferric alum and ferric chloride for tannins, alkalis for the anthraquinone derivatives and zinc chloriodide for cellulose and suberized tissue.

Identification Key.—Many of the powdered drugs, spices and other food products resemble each other closely as to form, color and other properties and it is therefore necessary that some outline for their identification be prepared. The most logical key for such a purpose is one based upon the histological characteristics of the powders and their reaction toward micro-chemical reagents. Keys based upon organoleptic observation, especially color, are unsatisfactory because of the rather wide variations which frequently exist. The key given herewith is based primarily upon the phloroglucin-hydrochloric acid test, the presence of starch and the presence of calcium oxalate, with further subdivisions depending upon anatomical characteristics. The key will be found helpful in practice and will render expeditious the examination of unknown powders.

Procedure.—After a preliminary examination the powder is mounted in phloroglucin-hydrochloric acid and the presence or absence of lignified tissue noted. The presence or absence of starch, if not already determined in the preliminary examination, is now to be determined and checked microscopically by means of water mounts. Calcium oxalate crystals are best seen in a chloral T.S. mount, and in this connection the micropolariscope will aid very materially. The suspected crystal is brought into focus with the analyzer so turned as to allow maximum light. The analyzer is then turned to such a position as to shut out all light from the field; the crystal will then appear brilliant against a black background. It must be remembered, however, that mechanical tissue and hairs often show similar deflection of polarized light. If calcium oxalate is suspected another mount is made in water and the crystals located. A drop or two of hydrochloric acid is then drawn under the cover-glass and its action upon the crystal observed. Calcium oxalate will dissolve without effervescence. The material most likely to be mistaken for calcium oxalate is sand. As a rule, sand shows no definite crystalline structure but may in some cases resemble that of prisms. It is *not* soluble in hydrochloric acid. In connection with the identification of calcium oxalate, the crystalline form, whether rosette aggregate, prismatic, raphide or sphenoidal microcrystalline, is observed.

With the determination of the presence or absence of lignified tissue, starch and calcium oxalate, the position of the unknown powder in one of the fundamental groups of the key is established. From now on it must be traced by a process of elimination depending upon the presence or absence of certain characteristic tissue elements. As an example, let us assume that we have found lignified tissue, starch and calcium oxalate in the form of rosettes present. Consulting the key, we next look for fibers and stone cells. Let us assume that we find relatively large stone cells but no fibers. This eliminates the groups headed "Fibers and Stone Cells present" and "Fibers present. Stone Cells absent" and brings us down to the group "Stone Cells present, Fibers absent," thus eliminating all but four possibilities. Upon measuring our stone cells we find them to be about 0.250 mm. in diameter. This identifies our unknown powder as granatum. After the powder has been identified by the use of the key, its description in the text should be consulted and a subsequent comparison made. Final comparison with an authentic sample cannot be too strongly urged.

Notes on the Key.—The key includes the more important U. S. P. and N. F. drugs occurring in powdered form, together with several other commonly occurring powdered substances. It is designed to be used in the identification of *pure* powders, and in this case the analyst must use discretion. A pure sample of bark drug contains no woody elements, yet in practice a small amount of woody tissue is occasionally found admixed with the drug. Such a drug is placed in the key under the heading "Tracheæ absent." In a similar manner stone cells in powdered clove, or rosettes of calcium oxalate in pimenta are occasionally found owing to admixture of stems.

As has been previously mentioned, color, odor and taste, while not adaptable as a means of forming subdivisions, are very useful as a check. The ultimate goal to be reached is the identification of the powder and the more ways in which this may be checked the more correct will be the result. In this connection too much stress cannot be laid upon special micro-chemical and other tests which may be found in the individual monographs in the text. Many drugs contain sublimable constituents which give characteristic crystals, and these in turn give characteristic reactions with reagents. The hydroquinone sublimed from uva ursi will give characteristic rod- and feather-like crystals which polarize light with a brilliant display of colors. The anthraquinones in rhubarb are readily sublimable and give the characteristic red reaction with alkalis. Micro-sublimation may be carried out as described early in the text.

It is also often expedient, as a check, to extract the powder with a suitable solvent and test the filtrate with such alkaloidal reagents as Mayer's or Wagner's, or for tannins with the various iron salt solutions. In certain cases the solvent may be evaporated and specific alkaloidal and other tests performed upon the residue. Among other special tests might be mentioned the potassium hydroxide test for conium, the various anthraquinone tests, the alcoholic-sulfuric acid test or the boric acid test for curcuma, the Grahe tests for cinchonas, the sclererythrin test for ergot and many others.

Mixtures.—The identification of the individual constituents in a mixture of powders is more difficult than the identification of a pure simple powder. The key will be found useful in this work, but discrepancies are bound to arise (such as the admixture of a starch with a non-starchy drug) and must be taken into consideration.

Adulteration.—Adulterated samples are to be treated as mixtures. Common adulteration of individual drugs has been discussed in the various monographs throughout the text and the analyst should note these carefully. Many of the substances used as adulterants are listed in the key. The quality of drugs is another matter and depends upon the quantity of active constituent present. This is determined by special methods, such as solvent extraction, alkaloidal and glucosidal assay, etc. In connection with the subject of adulteration these methods serve to detect admixture with exhausted powders of the same drug which cannot be detected microscopically.

In the study and identification of powdered drugs the care of reagents and the employment of careful technique cannot be too strongly urged. Reagents, slides and other apparatus must be scrupulously clean. Conclusions should not be formed hurriedly and in the course of an examination several similar mounts should be made as checks upon one another. The successful micro-analysis of powdered drugs depends more upon the personal care and observation of the analyst than upon any other factor.

KEY FOR THE IDENTIFICATION OF POWDERS

Lignified tissue present.

I. STARCH PRESENT.
  A. Calcium Oxalate Present
    a. In rosette aggregates.
      1. Fibers and stone cells present.
        (*a*) Crystal fibers present.
          α Powders light brown to olive brown.
            Red with alkalis.....................Cascara Sagrada
            Stone cells somewhat branching...........Wild Cherry
            Stone cells thick-walled up to 100 microns White Oak Bark
          β Powders dark brown.
            (1) Tracheæ present.
              Rosettes up to 95 microns. Bast characteristic. Tonga
            (2) Tracheæ absent.
              Stone cells up to 125 microns.............Juglans
        (*b*) Crystal fibers absent.
          α Tracheæ present.
            Fibers few. Stone cells up to 75 microns......Asclepias
            Fibers very few. Stone cells up to 750 microns. Corydalis
            Thick-walled lignified fibers...................Manaca
            Fibers thin-walled. Stone cells 40 to 200 microns Rumex (*crispus*)

Lignified tissue present.—(*Continued*).

I. STARCH PRESENT.
β Tracheæ absent.
(1) Fibers strongly lignified.
Bast numerous. Calcium oxalate mostly in prisms.................................Myrica
Bast few. Calcium oxalate mostly in rosettes..................Viburnum Prunifolium
Stone cells few. No prisms........Viburnum Opulus
(2) Fibers non-lignified.
Stone cells containing prisms................Cornus
Stone cells up to 190 microns..........Condurango
2. Fibers present. Stone cells absent.
(*a*) Tracheæ present.
α Starch abundant.
Thick-walled fibers in groups..................Althea
Resin cells present ....Ipomea
Bast long and narrow. Slightly lignified.......Stillingia
Fibers few, thin-walled............Rumex (*obtusifolius*)
β Starch grains few.
Simple hairs up to 900 microns...............Damiana
Glandular and non-glandular hairs present...Eriodictyon
(*b*) Tracheæ absent.
Bast strongly lignified, up to 1 mm.......Cotton Root Bark
Crystal fibers present..........................Frangula
Bast thick-walled...............................Rubus
3. Stone cells present. Fibers absent.
Stone cells numerous, 40 to 90 microns..............Canella
Stone cells 50 to 300 microns..............Pomegranate Bark
Stone cells few. Tannin masses......................Nutgall
Tracheæ present. Lignified hypodermal cells............Aralia
4. Fibers and stone cells absent.
(*a*) Tracheæ present.
Starch numerous..........................Podophyllum
Tannin masses. Large rosettes...............Geranium
Rosettes up to 150 microns. Red with KOH......Rhubarb
Resin cells present..............................Jalap
Characteristic glandular hairs. (Odor characteristic)........................Chenopodium
(*b*) Tracheæ absent.
Secretion cells. Lignified cork.................Euonymus
b. In prisms.
1. Fibers and stone cells present.
(*a*) Crystal fibers present.
α Powders light brown to olive brown.
(1) Rosettes also present.
Red with alkalis..................Cascara Sagrada
Stone cells branching, fibers few........Wild Cherry
Thick-walled stone cells up to 100 microns...................White Oak Bark
(2) No rosettes present.
Stone cells up to 150 microns.............Cocillana
Bast groups numerous.............Cascara Amarga
Prisms 35 to 200 microns................Quillaja
β Powder dark brown.
Stone cells up to 125 microns................Juglans

Lignified tissue present.—(*Continued*).

I. STARCH PRESENT.

(*b*) Crystal fibers absent.
α Tracheæ present.
Fiber tracheids present....................Gelsemium
β Tracheæ absent.
(1) Fibers strongly lignified.
Bast numerous. Calcium oxalate mostly in prisms.................................Myrica
Bast few. Calcium oxalate mostly in rosettes.................Viburnum Prunifolium
(2) Fibers non-lignified, or slightly lignified.
Stone cells containing prisms................Cornus
Stone cells up to 190 microns..........Condurango
Lignified cork cells, few......Northern Xanthoxylum
Lignified cork cells, numerous.Southern Xanthoxylum

2. Fibers present. Stone cells absent.
(*a*) Crystal fibers present.
α Tracheæ present.
(1) Starch abundant.
Fibers numerous. Cork present..Spanish Glycyrrhiza
Fibers numerous. Cork absent..Russian Glycyrrhiza
(2) Starch grains few.
Non-glandular hairs up to 600 microns......Galega
Entirely lignified. Crystal fibers few.Jamaica Quassia
Entirely lignified. Crystals few.....Surinam Quassia
β Tracheæ absent.
Crystal fibers short. Bast thin-walled...............Elm
(*b*) Crystal fibers absent.
α Fibers numerous.
Calcium oxalate mostly in rosettes ....Ipomea
Non-lignified wavy bast................. ...Krameria
β Fibers few.
Fibers only slightly lignified..................Calamus
Starch very small, 1 to 4 microns.......Cardamom Seed
Resin cells. Prisms up to 350 microns.....Iris Versicolor
Simple hairs up to 900 microns...............Damiana

3. Stone cells present. Fibers absent.
Stone cells few. Tannin masses.....................Nutgall
Stone cells 50 to 300 microns..............Pomegranate Bark
Starch up to 85 microns. Prisms in stone cells........Calumba

4. Fibers and stone cells absent.
(*a*) Tracheæ present.
Prisms up to 500 microns. Starch characteristic.....Orris
(*b*) Tracheæ absent.
Prisms up to 25 microns. Resin masses........White Pine

c. In raphides.
(*a*) Fibers present.
α Stone cells present.
(1) Tracheæ present.
iRaphides 50 to 135 microns...........Hydrangea
(2) Tracheæ absent.
Bast 0.3 to 1.5 mm. Odor characteristic.
With cork....................Saigon Cinnamon
Without cork.................Ceylon Cinnamon

Lignified tissue present.—(*Continued*).

I. Starch Present.
β Stone cells absent.
(1) Cork present.
(i) Raphides often over 50 microns
Slightly lignified fibers..........Veratrum Viride
(ii) Raphides less than 50 microns
Tracheids present.......................Ipecac
Fibers long..........................Phytolacca
Lignified cork..........................Helonias
(2) Cork absent.
(i) Fibers thick-walled.
Glandular hairs. Fibers numerous........Aletris
Fibers and raphides few...............Dioscorea
(ii) Fibers thin-walled.
Raphides up to 15 microns..........Sarsaparilla
Raphides up to 70 microns.........Cypripedium
(*b*) Fibers absent.
α Raphides up to 60 microns
Lignified endodermal cells............Convallaria Root
Stomata present............................Mitchella
β Raphides up to 225 microns
Mostly parenchyma ....Trillium
d. In sphenoidal microcrystals.
1. Tracheæ present.
(*a*) Fibers present.
Lignified wood, unlignified bast fibers..........Dulcamara
Starch characteristic..................Belladonna Root
Stone cells containing prisms...................Calumba
(*b*) Fibers absent.
Seed-coat tissue present.......................Solanum
Characteristic glandular hairs..............Chenopodium
2. Tracheæ absent.
Bast 0.30 to 1.35 mm..............................Cinchona
B. Calcium Oxalate Absent.
a. Fibers and stone cells present.
1. Tracheæ present.
(*a*) Stone cells numerous.
Odor slight. Stone cells in groups................Pareira
Odor characteristic. Palisade stone cells............Cubeb
Cystoliths present.............................Ruellia
(*b*) Stone cells few.
Characteristic starch........................Apocynum
2. Tracheæ absent.
Few short fibers............................Chionanthus
b. Fibers present. Stone cells absent.
1. Cork cells present.
(*a*) Odor aromatic.
α Hairs present.
Numerous thick-walled fibers......Euphorbia Pilulifera
Bast fibers few............................Zedoary
β Hairs absent.
Characteristic beaked starch..................Ginger
Fragments of oil canals...................Angelica Root
Characteristic bast up to 400 microns.........Sassafras
Valeric acid odor..........................Valerian
(*b*) Odor distinctive.
Starch 2 to 15 microns. Yellow powder..........Hydrastis

Lignified tissue present.—(*Continued*).

I. Starch Present.	
(*c*) Nearly odorless.	
Starch mostly simple	Caulophyllum
Starch 2- to 4-compound	Baptisia
2. Cork cells absent.	
(*a*) Hairs present.	
Starch numerous up to 7 microns	Coptis
Starch grains few 7 to 20 microns	Scoparius
(*b*) Hairs absent.	
α Resin cells (or resin) present.	
Starch compound up to 45 microns	Kava
Starch simple up to 9 microns	Leptandra
β Resin cells (or resin) absent.	
(1) Odor slight.	
Colors saliva yellow	Berberis
Starch 3 to 15 microns	Cimicifuga
Fibers few and non-lignified	Spigelia
(2) Odor distinct.	
Odor camphoraceous or terebinthinate	Serpentaria
c. Stone cells present. Fibers absent.	
Tabular stone cells, 100 to 400 microns	Aconite
Characteristic beaker cells. Starch very small	Black Pepper
Odor characteristic*	Allspice
d. Fibers and stone cells absent.	
1. Hairs present.	
Starch grains few. Oval tenacle heads, 100 to 200 microns	Drosera
Slightly lignified non-glandular hairs	Strophanthus
2. Hairs absent.	
(*a*) Tracheæ few.	
Red with alcoholic sulfuric acid	Curcuma
Characteristic starch grains	Colchicum Corm
Few beaked starch grains	Colchicum Seed
Latex cells. Starch characteristic	Sanguinaria
Odor characteristic. Starch blue with iodine	Nutmeg
Odor characteristic. Starch red with iodine	Mace
(*b*) Tracheæ frequent.	
α Cork present.	
Tracheæ up to 250 microns wide	Bryonia
β Cork absent.	
Odor characteristic	Asarum
Characteristic granular substance present	Sumbul
Characteristic scalariform tracheæ	Aspidium
II. Starch Absent.	
A. Calcium Oxalate Present.	
a. In rosette aggregates.	
1. Glandular and non-glandular hairs present.	
(*a*) Pollen grains numerous.	
Numerous T-hairs	Pyrethrum Flowers
Fibers up to 1 mm.	Hyoscyamus
Alcoholic extract red with KOH T.S.	Santonica
(*b*) Pollen grains few.	
Hairs up to 1 mm. Rosettes to 75 microns	Brayera
Large multicellular glandular hairs. (Lupulin.)	Humulus
Stellate cluster hairs up to 600 microns	Althea Leaves

---

* The presence of calcium oxalate rosettes indicate admixture with Allspice stems.

Lignified tissue present.—(*Continued*).

II. Starch Absent.
(*c*) Pollen absent.
Glandular hairs few........................Stramonium
Hairs up to 1 mm. Rosettes to 25 microns..Mallow Leaves
Twisted non-glandular hairs.................Eriodictyon
Cystoliths present in hairs.....................Cannabis
2. Only non-glandular hairs present.
(*a*) Pollen grains numerous.
Chromoplasts present.........................Calendula
Mechanical elements numerous...............Centaurium
(*b*) Pollen grains few.
Stem tissues numerous.......................Passiflora
(*c*) Pollen absent.
α Crystal fibers present.
Thick papillose hairs...........................Senna
Hairs characteristic.........................Castanea
β Crystal fibers absent.
Hairs few...Buchu
Rosettes in aleurone grains.......................Anise
Characteristic stone cells............................Tea
Simple hairs up to 900 microns...............Damiana
3. Only glandular hairs present.
Hairs containing rosettes of calcium oxalate........Grindelia
Odor characteristic............................Matricaria
4. Hairs absent.
(*a*) Calcium oxalate rosettes in aleurone grains.*
α Rosettes, 1 to 5 microns
Wavy-walled epidermal cells..................Caraway
Oil tubes, 100 to 200 microns wide.............Fennel
β Rosettes, 2 to 10 microns
Epidermis slightly papillose...............Celery Fruit
Elongated polygonal epidermal cells..........Coriander
Spongy parenchyma characteristic.......Angelica Fruit
Characteristic odor with KOH T.S..............Conium
(*b*) Pollen present.
Pollen grains tetrahedral†............................Clove
(*c*) Pollen absent.
α Odor characteristic.
Bast slightly lignified......................Eucalyptus
β Odor slight.
Epidermal tissues characteristic............Chimaphila
Red with alkalis. Stone cells characteristic.......................Rhamnus Cathartica
b. In prisms.
1. Glandular and non-glandular hairs present.
Crystal fibers present............................Melilotus
Fibers up to 1 mm.............................Hyoscyamus
Hairs up to 1 mm. Crystals mostly rosettes...........Brayera
2. Only non-glandular hairs present.
(*a*) Pollen present.
Chromoplasts present.........................Calendula
Mechanical elements numerous...............Centaurium
Non-glandular hairs characteristic..............Trifolium
Thick-walled hairs up to 600 microns..............Galega

---

* All members of this group possess a characteristic odor.

† Bast fibers present in Clove powder indicate the presence of stems. Starch grains indicate the presence of clove fruits.

Lignified tissue present.—(*Continued*).

II, Starch Absent.
(*b*) Pollen absent.
Multicellular stellate hairs............Witch Hazel Leaves
Red with alkalis.................................Senna
Tannin (ammonio-ferric alum test).......Chestnut Leaves
Characteristic jointed hairs.......................Matico
3. Hairs absent.
(*a*) Only xylem tissues present.
Ether extract orange-yellow, green fluorescence..................................Red Saunders
Aqueous extract purple with alkalis ....Hematoxylon
Occasionally a few starch grains. Bitter...........Quassia
(*b*) Other tissues also present.
Yellow with NaOH T.S...............Bitter Orange Peel
Characteristic sublimable hydroquinone..........Uva Ursi
Bast slightly lignified.........................Eucalyptus
Stone cells to 145 microns......................Juniper
c. In raphides.
Raphides up to 1 mm..................................Squill
d. In sphenoidal microcrystals.
1. Microcrystals only.
Pollen grains few..........................Belladonna Leaf
Seed-coat fragments numerous......................Solanum
Non-glandular hairs numerous......................Tobacco
2. Rosettes numerous.............................Stramonium
3. Prisms present.
Non-glandular hairs 1- to 10-celled...............Hyoscyamus
Characteristic jointed hairs..........................Matico
B. Calcium Oxalate Absent.
a. Glandular and non-glandular hairs present.
1. Pollen present.
(*a*) Odor mint-like and characteristic.
α Non-glandular hairs 1- to 8-celled.
Crystals in glandular hairs.................Peppermint
No crystals in glandular hairs...............Spearmint
β Non-glandular hairs not over 5-celled.
Non-glandular hairs, 1 to 5 cells...............Catnep
Non-glandular hairs, 2 to 3 cells.............Pennyroyal
(*b*) Odor not mint-like.
α Pollen grains spiny.
Non-glandular hairs, 3 kinds.....................Arnica
Corolla tissues numerous.................Eupatorium
Non-glandular hairs twisted................Horehound
Non-porous thin-walled fibers...................Tansy
β Pollen grains smooth.
Odor slight..............................Scutellaria
Odor characteristic...........................Thyme
2. Pollen grains absent.
(1) Greenish powders.
Non-glandular hairs uniseriate..................Digitalis
Non-glandular hairs branching............Mullein Leaves
Non-glandular hairs parallel with leaf surface........Sage
(2) Reddish-brown powder.
Small stone cells of endocarp................Rhus Glabra
b. Only non-glandular hairs present.
1. Pollen present.
Non-glandular hairs occasional......................Lobelia
Aqueous solution golden-yellow.................Chelidonium

Lignified tissue present.—(*Continued*).

II. STARCH ABSENT.
2. Pollen grains few.
Simple thick-walled hairs up to 2.5 mm. . . . . Pulsatilla
Twisted multicellular hairs. . . . . Senecio
Long unicellular hairs. . . . . Scoparius
3. Pollen absent.
Cystoliths present. . . . . Boldus
Hairs characteristic. . . . . Farfara
Hairs few in spreading clusters. . . . . Ignatia
Strongly lignified characteristic hairs. . . . . Nux Vomica
c. Only glandular hairs present.
Oval tentacle heads characteristic. . . . . Drosera
d. Hairs absent.
1. Fibers and stone cells present.
Stone cells, 18 to 42 microns. . . . . Echinacea
Odor characteristic. . . . . Xanthoxylum Fruits
Characteristic stone cells. . . . . Star Anise
2. Fibers present. Stone cells absent.
(*a*) Pollen present.
Tracheæ numerous. . . . . Chirata
(*b*) Pollen absent.
α Stomata present.
Abundant pith parenchyma. Adonis
Lignified stomata. . . . . Thuja
β Stomata absent.
Short wood fibers. . . . . Senega
Strongly lignified wood fibers. Inula
Unlignified intermediate fibers. . . . . Taraxacum
Wood fibers few. Resin cells. . . . . Lappa
Lignified epidermal cells. . . . . Triticum
3. Stone cells present. Fibers absent.
(*a*) Odor characteristic.
α Oily mounts.
Numerous oil globules. . . . . Linseed
Wavy-walled stone cells. . . . . Capsicum
Stone cells up to 1 mm. . . . . Coffee
β Mucilaginous mount.
Stone cells polygonal. . . . . Fenugreek
(*b*) Odor slight (when dry).
Stone cells uniformly thickened. Pepo
Seed-coat fragments characteristic. . . . . Black Mustard
Same, lacking brown pigment cells. . . . . White Mustard
Mostly parenchyma*. . . . . Colocynth
Mostly stone cells . . . . Nut shells, olive pits, etc.
4. Stone cells and fibers absent.
(*a*) Aleurone grains present.
Seed-coat cells with beaded walls. . . . . Delphinium
Aleurone grains up to 50 microns. . . . . Cocculus
Aleurone grains alone present. . . . . Mustard Flour
(*b*) Aleurone grains absent.
Tracheæ scalariform and reticulate. . . . . Gentian

---

* Stone cells indicate the presence of seeds.

Lignified tissue absent.

I. VEGETABLE TISSUE PRESENT.

A. Powders Reddish, Brownish or Yellowish.

a. Unaltered starch grains present.
Oil globules numerous. Odor characteristic...............Cacao
Starch grains, 10 to 60 microns.......................Galanga

b. Altered starch grains present.
Gold chloride test characteristic........................Guarana
Parenchyma with brownish walls.........................Kola

c. Starch grains few.
Non-porous bast fibers numerous...................Mezereum
Green with ferric chloride..............................Gambir

d. No starch present.

1. Consisting of hairs only.
Large glandular hairs..............................Lupulin
Glandular and non-glandular hairs...................Kamala
Hairs with short, recurved, pointed protuberances......Mucuna

2. Consisting principally of spores.
Characteristic spores; tetrahedral, 25 to 40 microns. Lycopodium
Spores about 7 microns.........................Ustilago

3. Consisting principally of pollen grains.
Characteristic winged pollen grains....Pollen of Pine species

4. Consisting principally of parenchyma or mycelial tissue.
Characteristic sclererythrin test......................Ergot
Calcium oxalate prisms, 10 to 40 microns. Mycelia......Agaric
Epidermal tissue and pseudo-parenchyma..............Fucus

B. Whitish Powders.
Polygonal starch grains, 10 to 35 microns...............Corn meal
Starch grains, 5 to 40 microns.........................Wheat flour
Thick-walled hairs with narrow lumen............Wheat middlings
Starch grains, 20 to 60 microns..........................Rye flour
Thick-walled hairs with large lumen.................Rye middlings
Starch, 5 to 25 microns............................Barley flour
Sclerenchyma fibers with brown contents..........Buckwheat flour
Hairs broader in the middle ... .Oatmeal

II. VEGETABLE TISSUE ABSENT.

A. Only Unaltered Starch Grains Present.

a. Ovoid grains mostly simple.
Excentric circular hilum.........................Potato starch
Excentric fissured hilum.......................Maranta starch

b. Polygonal grains.
Starch grains, 10 to 35 microns....................Corn starch
Starch grains, 2 to 10 microns.....................Rice starch

c. Lenticular grains.
Starch grains, 5 to 25 microns...................Barley starch
Starch grains, 5 to 40 microns...................Wheat starch
Starch grains, 20 to 60 microns....................Rye starch

d. Reniform grains...........................Leguminous starches

e. Characteristic grains...........................Other starches

B. Altered Starch Grains Present.
Becoming pasty on addition of cold water.................Dextrin
Becoming pasty with hot water.............................Sago
Disintegrates with water.......................Sago (Imitation)

C. Starch Grains and Mucilage Present.
Swells in water.................................Tragacanth

Lignified tissue absent.—(*Continued*).

- II. VEGETABLE TISSUE ABSENT.
  - *D*. No Starch Present.
    - *a*. White Powders.
      - 1. Soluble in water.
        - Forming a mucilage with water........................Acacia
        - Monoclinic prisms................................Sucrose
        - Gritty particles. Monoclinic prisms. Red with H_2SO_4...Lactose
      - 2. Insoluble in water.
        - (*a*) Soapy feel.
          - Broken crystals..................................Talc
        - (*b*) Soluble in acetic acid.
          - α With effervescence.
            - Prisms or irregular angular fragments............Precipitated Calcium Carbonate
            - Amorphous powder....................Prepared Chalk
            - Rhombic crystals or irregular fragments........................Barium Carbonate
          - β Without effervescence.
            - Rounded masses......................Heavy Magnesia
            - Very light..........................Light Magnesia
        - (*c*) Insoluble in acetic acid (but soluble in nitric acid).
          - Tetragonal or cubical crystals...............Precipitated Calcium Phosphate
          - Acicular crystals........................Calcium Sulfate
          - Rhombic prisms or crystals of various sizes..Barium Sulfate
          - Irregular fragments.........................Terra Alba
        - (*d*) Consisting of diatoms...................Infusorial Earth
    - *b*. Yellow Powders.
      - 1. Giving off odor of sulfur dioxide on heating.
        - Rounded masses in chains....................Washed Sulfur
        - Rounded masses in irregular groups........Precipitated Sulfur
      - 2. No odor of sulfur dioxide on heating.
        - (*a*) Nearly colorless in glycerin mount.
          - Transparent irregular masses....................Mastic
        - (*b*) Yellowish in glycerin mount.
          - α Containing oil globules.
            - Irregular masses........................Scammony
          - β Transparent or translucent.
            - Soluble in cold alcohol. Green with copper acetate..Rosin
            - Insoluble in cold alcohol. No green color with copper acetate..........................Sandarac
            - Reddish with alkalis.....................Aloe (Cape)
          - γ More opaque.
            - Light or grayish particles.................Ammoniac
            - Yellowish particles........................Gamboge
    - *c*. Brownish powders.
      - 1. With occasional cellular tissue*.........................Opium
      - 2. Without cellular tissue.
        - (*a*) Possessing oil.
          - Grayish fragments..........................Asafetida
          - Yellowish or yellowish brown fragments...........Myrrh

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* Opium may contain tissues from the poppy capsule, or from the leaves of *Rumex* species in which it is occasionally packed. If a diluent has been added its microscopic characteristics will also be evident.

Lignified tissue absent.—(*Continued*).

II. VEGETABLE TISSUE ABSENT.

- (*b*) Without oil.
  - α Remaining opaque in glycerin.
    - Red with alkalis......................Aloe (Socotrine)
    - Characteristic odor, and sublimate.............Benzoin
    - Grayish opaque fragments................Elaterinum
    - Brownish angular fragments..............Lactucarium
  - β More or less translucent in glycerin.
    - Yellowish brown. Red with alkalis. Finally green with HNO_3......................Aloe (Cape)
    - Dark brown. Red with alkalis. Red with HNO_3............................Aloe (Curaçao)
    - Yellowish brown. Red with alkalis. Yellow with HNO_3.........................Aloe (Socotrine)
    - Acicular crystals. Green with ferric chloride......Gambir
    - With rhombohedral crystals...................Catechu
    - Fragments translucent, deep red.................Kino
    - Microcrystalline. Red with alkalis..........Chrysarobin

INDEX

A

- *Abies balsamea*, 107, 204
  - *pectinata*, 107
  - *siberica*, 111
- Abrus, 360
  - *precatorius*, 333, 360
- Absinthe, 643
- Absinthiin, 644
- Absinthium, 643
- Absolute alcohol, 137
- Absorbent cotton, 425
  - gauze, 427
- *Abuta amara*, 261
  - *rufescens*, 261
- Abyssinian cardamom, 184
- Acacia, 351, 370
  - *arabica*, 353
  - *catechu*, 358
  - *decurrens*, 353
  - *ehrenbergiana*, 353
  - *giraffæ*, 353
  - *homalophylla*, 353
  - *horrida*, 353
  - *pycnantha*, 353
  - *senegal*, 351
  - *seyal*, 353
  - *stenocarpa*, 353
  - *suma*, 358
- *Acer nigrum*, 409
  - *saccharinum*, 409
  - *saccharum*, 136, 408
  - *spicatum*, 409, 614
- *Aceraceæ*, 408
- *Aceras anthropophora*, 188
- Acetyltannic acid, 215
- Achilles, 645
  - *millefolium*, 645
  - *moschata*, 645
  - *tobilis*, 645
  - *anacetifolia*, 645
- *Achras sapota*, 483
- Acid ammonium valerate, 616
- *Acipenser huso*, 679
- Aconite, 238, 725
  - leaves, 240
  - root, 238
- Aconitine, 239
- *Aconitum balfourii*, 241
  - *chasmanthum*, 241
  - *deinorhizum*, 241
  - *ferox*, 241
  - *fischeri*, 241
  - *heterophyllum*, 241
  - *laciniatum*, 241
  - *lycoctonum*, 241
  - *napellus*, 238, 240
  - *spicatum*, 241
  - *stærckianum*, 241
  - *uncinatum*, var. *japonicum*, 241
- Acorns, 211
- *Acorus calamus*, 148, 149
- Acrinyl isothiocyanate, 302
- *Actinomyces griseus*, 79
- *Actinostrobus pyramidalis*, 108
- Activated charcoal, 206
  - ergosterol, 666
- Addison's disease, 708
- Aden senna, 347
- Adhesive absorbent gauze, 427
  - gauze, 427
- Adiantum, 98
  - *capillus-veneris*, 98
  - *pedatum*, 98
- Adonidin, 249
- Adonis, 249, 728
  - *æstivalis*, 250
  - *microcarpa*, 250
  - *vernalis*, 249
- Adrenal cortex, 706, 707
  - active hormones, 706-708
  - functions, 706–708
  - hyperactivity, 708
  - hypoactivity, 707
  - preparations, 708
  - therapeutic use, 708
- Adrenal Cortex Extract, N.-N.R., 708
- Adrenal glands, 706
  - medulla, 706
    - active hormone, 706
    - functions, 706
- Adrenalin, U.S.P., 707
- Adulteration of drugs, 34, 721
- *Ægle marmelos*, 377
- Æsculin, 310
- Æthusa, 470
  - *cynapium*, 470
- *Aframomum angustifolium*, 184
  - *hanburii*, 184
  - *korarima*, 184
  - *mala*, 184
  - *melegueta*, 184
- African bdellium, 389
  - cannabis, 221
  - capsicum, 569
  - cayenne, 569
  - chillies, 568
  - copaiba, 349
  - ginger, 177
  - kino, 336
  - myrrh, 387
  - nutmeg, 266
  - red-wood, 337
  - rubber, 401
  - sandalwood, 337
- Agar, 82
- Agaric, 91, 729
  - larch, 91
  - white, 91
- Agaricus, 91
  - *campestris*, 92
- *Agropyron repens*, 140
- *Agrostis alba*, 649
- Ajowan oil, 535
- Alantol, 636
- Alban, 483
- Albumin tannate, 215, 680
- Albutannin, 680
- Alcohol, 137
- Aletris, 168, 724
  - farinosa, 168
- Alexandria senna, 344, 345
- Alfalfa, 360
  - hay, 360
  - meal, 360
- *Algæ*, 80
- Algin, 82
- Alicante anise, 460
- Alizarin, 311, 610
- Alkaloids, 49, 591
  - cinchona, 600
  - derivatives of isoquinoline, 595
    - of quinoline, 594
  - glyoxaline group, 594
  - group containing aliphatic bases with an aromatic nucleus, 593
  - indole derivatives, 595
  - of unknown constitution, 596
  - opium, 287
  - phenanthrene, 595
  - purine bases, 595
  - pyridine group, 593
  - pyrrolidine group, 593
  - with condensed pyrrolidine and piperidine rings, 594
- Alkanet, 520
- Alkanna, 520
  - *tinctoria*, 520
- Allergenic preparations, 647
- Allium, 162
  - *macleanii*, 192
  - *sativum*, 162
- Allspice, 454, 725
  - grown, 455
  - Mexican, 454
- Allyl isothiocyanate, 298, 303
- Almond, 316
  - bitter, 316
  - cake, 317
  - meal, 317
  - oil, bitter, 316
    - expressed, 318
    - sweet, 316
  - sweet, 318
- Aloe, 156
  - *africans*, 156
  - *barbadensis*, 156, 160
  - *Barbadoes*, 156
  - cape, 156, 730, 731
  - *chinensis*, 156
  - color tests for, 159
  - Curaçao, 156, 731
  - *ferox*, 156
  - leaf, 160
  - *Perryi*, 156
  - *socotrina*, 156
  - socotrine, 156, 731
  - *spicata*, 156
  - *vera*, 156, 157
  - *vulgaris*, 156
- Aloe-emodin, 159, 414
- Aloe-emodinanthranol, 159

Aloe-resinoltannol, 103
Aloin, 158
Alphahypophamine, 699
Alpinia officinarum, 179
Althea, 422, 722
  flowers, 425
  leaves, 425, 725
  root, 422
Althæa officinalis, 422, 425
  rosea, 425
Altingia excelsa, 306
Alum-precipitated diphtheria toxoid, 73
  tetanus toxoid, 73
Alum root, 304
Aluminum alginate, 82
Alypin hydrochloride, 367
Ambergris, 681
Ambrosia artemisiifolia, 649
  bidentata, 649
  elatior, 649
  psilostachya, 649
  trifida, 649
American arrowroot, 185
  blistering beetle, 660
  blue vervain, 521
  calumba, 259
  centaury, 504
  elder, 614
  gentian, 503
  hellebore, 150, 251
  hemp, 219
  ipecac, 607
  isinglass, 679
  licorice, 333
  mastic, 404
  nutgalls, 213
  pennyroyal, 544
  saffron, 174
  sarsaparilla, 457
  senna, 347
  spikenard, 456
  storax, 314
  turpentine oil, 105, 106, 108
  wormseed, 233
Amethocaine hydrochloride, 369
Aminoacetic acid, 688
Aminophylline, 435
Ammoniac, 474, 730
Ammoniated glycyrrhizin, 332
Amniotin, N.N.R., 711
Amœba, 651
Amolonin, 312
Amomum aromaticum, 184
  cardamomum, 184
  maximum, 184
  xanthoides, 184
Amorphous aconitine, 239
Amydricaine hydrochloride, 367
Amygdalin, 310, 312, 315, 317, 318
Amygdalus communis, 316
    var. *amara*, 316
    var. *dulcis*, 316, 319
Amylase, 690, 692
Amylcaine hydrochloride, 367
Amylolytic enzymes, 690
✓Amylopsin, 690, 692
Amylum, 133
Amyris balsamifera, 223
Anacardiaceæ, 403
Anacardium, 406
  coccidentale, 406
Anacyclus officinarum, 643
Anacyclus pyrethrum, 643
Analytical pharmacognosy, 51
Anamirta cocculus, 262
  paniculata, 262
Anatoxin-Ramon, 73
Anchietea salutaris, 607
Anchusæ tinctoriæ radix, 520
Andria araroba, 339
Androgens, androsterone, 686
  hyperactivity, 709
  hypoactivity, 709
  preparations, 709
  testosterone, 686
  therapeutic uses, 709
Andropogon nardus, 141
  squarrosus, 141
Androsterone, 686
Anemone patens, 249
  pratensis, 249
  pulsatilla, 249
Anemonin, 249
Anesthesin, 370
Anethi fructus, 471
Anethol, 2, 263, 460. *See* Anethole.
Anethole, 263, 460, 462
Anethum graveolens, 471
Aneurine Hydrochloride, U.S.P., 678
Angelica, 471
  archangelica, 471
  fruit, 471, 726
  herb, 471
  oil, 472
  root, 471, 724
  seed, 471
  tree, 458
Angiosperms, 119
Angostura bark, 383
Anhalonium, 446
Anhydro-hydroxyprogesterone, U.S.P., 713
Anhydrous d-mannitol, 135
  lanolin, 685
Animal charcoal, 693
  drugs, 24, 651
✓Anise, 460, 726
  alicante, 460
  bay, oil, 456
  Chinese, 263
    oil, 462
  Japanese star, 263
  oil, 462
  Russian, 460
  star, 263
    oil, 462
Aniseed, 460
  buchu, 378
Annatto, 438
  family, 438
Annulata, 651
Anogeissus latifolia, 353
Anterior lobe of pituitary body, 700
  Pituitary, N.F., 702
Anthemis, 626
  arvensis, 626
  cotula, 626
  nobilis, 626
  oil, 628
Anthocyanins, 312
Anthoxanthins, 312
Anthoxanthum odoratum, 343, 649
✓Anthraquinones, 311
Antibacterial serums, 76
Antibiotics, 50, 78
  agents, 78
Antidiphtheric globulins, 74
Antimeningococcic serum, 76
Antipneumococcic serum, 76
Antirabic vaccine, 67
Anti-scarlet fever globulins, 75
Antitetanic globulins, 75
Antitoxic serums, 74
Antitoxin, 74
  diphtheria, 74
  gas gangrene, 75
  scarlet fever, 75
  tetanus, 75
Antivenins, 74, 76
  antivenin Cascabel, 76
  Bothrops, 76
  North American, 76
  tropical American, 76
    rattler, 76
Apidæ family, 660
Apigenin, 311
Apiol, 470
Apis mellifera, 660, 661
Apium graveolens, 468
Apoatropine, 555
Apocynaceæ, 505
Apocynin, 506
Apocynum, 505, 724
  androsæmifolium, 505, 507
  cannabinum, 505, 507
Apomorphine hydrochloride, 287, 288
Apothesine hydrochloride, 368
Applied bacteriology, 78
Apricot kernel oil, 319
Aquifoliaceæ, 407
Arabian myrrh, 387
  senna, 347
Arabic acid, 335, 352
Arabin, 352
Arabinose, 134, 135
Araceæ, 148
Arachidic acid, 395
Arachis hypogæa, 355
Arachnoidiscus ehrenbergii, 83
Aralia, 456, 722
  montana, 459
  nudicaulis, 168, 457
  racemosa, 168, 456
  spinosa, 168, 382, 458
Araliaceæ, 456
Araliin, 459
Arasina gurgi, 438
Arbor vitæ, 114
Arbutin, 309, 478, 479
Archil, 94
Arctium lappa, 637
  lappæ semina, 638
  minus, 637
Arctostaphylos uva-ursi, 477
Areca, 144
  catechu, 144
  nut, 144
Arecoline hydrobromide, 146
Argel leaves, 347
Argemone mexicana, 256
Argol, 422
Arisæma triphyllum, 150
Aristolochia reticulata, 224
  serpentaria, 224
Aristolochiaceæ, 223
Arnica, 624, 727
  American, 624
  cordifolia, 624

Arnica, European, 624
  flowers, 624
  fulgens, 624
  Montana, 624
  plant, 624
  sororia, 624
Arnicin, 624
Arnotta, 438
Aromatic powder, 274
Arrowroot, 185
  American, 185
  Bermuda, 185
  Brazilian, 185
  East Indian, 185
  family, 184
  St. Vincent, 185
  starch, 185
  South Sea Island, 185
  Tahiti, 185
Artemisia absinthium, 643
  Cina, 629
  frigida, 279
  gallica, 630
  trifolium, 279
Arthropoda, 652
Artificial oil of sassafras, 279
Arum, 150
  family, 148
  maculatum, 150
Asafetida, 473, 730
Asarum, 226, 725
  canadense, 226, 227
Aschheim-Zondek pregnancy test, 703
Ascitic fluid, 689
Asclepiadaceæ, 511
Asclepiadin, 513
Asclepias, 513, 721
  currasavica, 607
  incarnata, 513
  seriaca, 513
  syriaca, 513
  tuberosa, 513
Ascorbic Acid, U.S.P., 675, 679
    Tablets, U.S.P., 679
Asparagin, 423
Aspidium, 97, 725
Aspidosperma, 511
  quebracho blanco, 511
  colorado, 511
Aspidospermine, 511
Assam gum, 390
Astragalus crotalaria, 360
  gummifer, 334
  mucronata, 335
  sarcocolla, 335
Athyrium filix-fœmina, 98
Atropa belladonna, 547, 554, 555
Atropamine, 555
Atropine, 553, 554, 563, 564, 594
  sulfate, 555
Attar of rose, 324
Aurantiamaric acid, 372
Aurantiamarin, 372
Aurantin, 372
Australian gum, 353
  kino, 336, 450
  tobacco, 565
Austrian turpentine oil, 109
Avena, 139
  sativa, 120, 139
Avenæ farina, 139
Aves, 679
Azadirachta indica, 390
Azedarach, 390
  Indian, 390
Azolitmin, 95

B

Baccæ spinæ cervinæ, 418
Bacillariaceæ, 80
Bacillus brevis, 80
  lepræ, 439
  tuberculosis, 439
Bacteria, 66
Bacterial vaccines, 68
Bacterins, 68
Bacteriologics, 50
Bacteriophage, 70
Bacterium lactis, 688
Bael fruit, 377
Bahia rubber, 401
Balata, 483
Ballota hirsuta, 543
  nigra, 543
Balm, 546
  of Gilead buds, 203
    false, 204
Balsam, 48, 104, 349
  copaiba, 349
  of fir, 107
  of Peru, 337
  of tolu, 338
  microchemistry of the, 486
  poplar buds, 203
Balsamic resins, 48
Bangalore gum, 390
Baphia nitida, 337
Baptisia, 358, 725
  tinctoria, 358
Baptisin, 310, 358
Barbadoes, 156
Barberry, 252
  bark, 256
  family, 256
Barfoed test, the, 132
Barium carbonate, 730
  sulfate, 730
Barley, 138
  flour, 139, 729
  starch, 120, 124, 729
Barosma betulina, 377, 378
  crenulata, 377
  pulchella, 378
  serratifolia, 377
Barwood, 337
Bassorin, 335
Bastard cardamom, 184
  ipecac, 607
Batavia cinnamon, 271, 274
Bayberry bark, 206
Bay laurel, 282
Bdellium, 389
  African, 389
  Indian, 389
  opaque, 389
Bearberry, 477
Bear's-foot hellebore, 251
Bebeerine, 261
Bebeeru bark, 261
Bee balm, 536
Beech, 209
  family, 209
  nuts, 210
Beechwood, 210
  creosote, 210
  tar, 210
Beef, 688
  extract, 688
  heart, 689
  liver, 689
Beeswax, 661
Beet, 233
Belladonna, 547
  leaf, 547, 727
  root, 547, 724
Belladonnine, 556, 594
Bengal cardamoms, 184
  kino, 336
  quince, 377
Benne leaves, 587
  oil, 587
Benzaldehyde, 319
Benzestrol, N.N.R., 711
Benzocaine, 370
Benzoic acid, 486
Benzoin, 483, 731
  Palembang, 486
  Penang, 486
  Siam, 483
  Styrax, 483, 484
  Sumatra, 483
Benzoinated lard, 692
Benzoresin, 485
Benzoresinol, 485
Benzyl cinnamate, 338
Berberidaceæ, 252
Berberine, 243, 244, 250, 25
  256, 259, 595
Berberis, 254, 256, 725
  aquifolium, 254
  asiatica, 256
  Baccæ, 256
  canadensis, 256
  vulgaris, 256
Bergamot oil, 376
Bermuda arrowroot, 185
    starch, 120
  grass, 140, 141
Betaeucaine hydrochloride. 368
Beta saccharifera, 136
  vulgaris, 233
Betahypophamine, 699
Betel nut, 144
Bethroot, 171
Betula alba, 209
  lenta, 209, 481
  oil, 481
  pendula, 209
Betulaceæ, 209
Bichy nut, 432
Bile acids, 686
    cholic, 686
    glycocholic, 686
    taurocholic, 686
Biological evaluation of drugs 43
Biotin, 672
Birch bark, 209
  family, 209
Bird's-foot violet, 441
Birthwort family, 223
Bisadol, 389
Bissy-bissy nut, 432
Bistorta, 233
Bitter almond, 316
    oil, 319
  apple, 617
  chocolate, 430
  fennel, 463
  orange oil, 373
    peel, 372, 727

- Bitter polygala, 393
- Bitterwood, 384
- Bivalent gas gangrene antitoxin, 75
- *Bixa orellana*, 438
- *Bixaceæ*, 438
- Black alder, 407
  - caraway, 466
  - catechu, 358
  - cohosh, 245
  - cutch, 358
  - hellebore, 153, 250
  - horehound, 543
  - Indian hemp, 505
  - mustard, 298, 728
  - nightshade, 566
  - oak bark, 211
  - pepper, 195, 725
  - poplar, 206
  - raspberries, 323
  - sassafras, 276
  - snakeroot, 245
  - tea, 435
- Blackberries, 323
- Blackberry bark, 323
  - syrup, 323
  - wine, 323
- Blackhaw, 610
- Bladderwrack, 82
- Blazing star, 170
- Bleached beeswax, 661
- Blistering flies, 658
- Blood, 689
- Bloodroot, 290
- Blue cohosh, 256
  - dandelion root, 636
  - flag, 175
  - gentian, 503
- Bluebell family, 621
- *Blumea balsamifera*, 279
- *Bocconia*, 282
- Boldo, 269
- *Boldu boldus*, 269
- Boldus, 269, 728
- *Boletus ingarius*, 92
- Bombay chillies, 569
  - coriander, 468
  - mace, 267
- Bone, 693
- Boneset, 632
- Borage family, 520
- *Boraginaceæ*, 520
- Borago, 521
  - *officinalis*, 521
- Bordeaux turpentine, 106
- Borneo camphor, 279
  - rubber, 401
- Borneol, 279, 535
- Bornträger's test, 159
- *Bos indicus*, 684
  - *taurus*, 683, 684, 686, 687, 689, 690, 692
- *Boswellia carterii*, 389
- Botanical origin of drugs, 14
  - source of drugs, 14
- Botany Bay kino, 450
- Bourbon vanilla, 187
- Bovidæ, 683
- Boxwood, 262
- Bran, 127
- Brandy, 421, 422
- *Brassica alba*, 295, 301
  - *arvensis*, 296, 300
  - *besseriana*, 296, 301
  - *campestris*, 297, 302
  - *cernua*, 297, 302
- *Brassica chinensis*, 297, 302
  - *glauca*, 297, 302
  - *juncea*, 296, 298, 303
  - *nigra*, 295, 296, 298, 299, 301, 303
  - *napus*, 296, 301
  - *oleracea*, 296
  - *rapa*, 297, 301
- Brayera, 327, 725, 726
- Brazil wood, 357
- Brazilian arrowroot, 185, 402
  - ipecac, 603
  - jalap, 515
  - vanilla, 187
- Brazilin, 357
- Breakfast cocoa, 430
- Brewer's yeast, 86, 87
- British gum, 126
- Broom tops, 341
- Brown algæ, 80
  - mustard, 298
- Brucine, 491, 493, 495, 595
  - sulfate, 491, 493
- Brunfelsia hopeana, 568
- Bryonia, 619, 725
  - *alba*, 619
  - *dioica*, 619
- Bryonidin, 620
- Bryonin, 620
- Bryony, 619
- *Bryophyta*, 96
- Bryophytes, 96
- Buchu, 377, 726 ✓
  - camphor, 378
- Buckbean, 504
- Buckthorn bark, 416
  - berries, 418
  - family, 410
- Buckwheat family, 227
  - flour, 729
  - starch, 120
- Bugleweed, 543
- Buna N, 401
  - S, 401
- Burbot liver oil, 664, 678
- Burdock fruit (seed), 638
  - root, 637
- Burgundy pitch, 108
- Burnt sponge, 651
  - sugar coloring, 136
- *Burseraceæ*, 387
- Butacaine sulfate, 368
- Butadiene-1, 401
- Butamin, 368
- *Butea frondosa*, 336
  - kino, 336
- Butesin, 370
  - picrate, 370
- Butter, 687
- Butterfly weed, 513
- Buttermilk, 687
- Butternut bark, 207
- Button snakeroot, 471
- Butyl aminobenzoate, 370
- Butyn sulfate, 368
- Butyric acid, 520
- Buxus sempervirens, 262

C

- CACAO, 431, 729
  - beans, 429, 430
  - butter, 430, 431
  - prepared, 430
  - seeds, 429, 430
- Cacao shells, 430
- *Cactaceæ*, 444
- Cactus family, 444
  - grandiflorus, 445
- *Cæsalpinaceæ*, 329
- *Cæsalpinia echinata*, 357
  - *sappan*, 357
- Caffea, 608
  - tosta, 608
- Caffeine, 409, 432, 433, 435, 609
  - and sodium benzoate, 434
    - salicylate, 434
  - sodio-benzoate, 434
    - -salicylate, 434
- Cajuput oil, 452
- Calabar bean, 340
- Calamus, 723
  - *draco*, 147, 148
- Calciferol, 666, 667
- Calcium carbonate, precipitated, 730
  - gluconate, 135
  - levulinate, 135
  - pantothenate dextrorotatory, 672
  - phosphate, precipitated, 730
  - sulfate, 730
- Calcutta ginger, 177
- Calendula, 628, 726
  - *officinalis*, 624, 628
- Calf's brain, 689
- Calicut ginger, 177
- Californaia gar, 82
  - oak galls, 213
- Calisaya bark, 596
- *Callitris quadrivalvis*, 108
- *Calluna vulgaris*, 479
- *Caltha palustris*, 245
- Caltrop family, 370
- ✓ Calumba, 258, 723, 724
  - rhizome, 259
- *Camelina sativa*, 363
- Cameroon cardamom, 184
- *Campanulaceæ*, 621
- Camphor, 276
  - Borneo, 279
  - monobromated, 278
  - Ngai, 279
  - oil, 279
    - Formosa, 279
    - light, 279
    - white, 279
  - synthetic, 276
- Cam-wood, 337
- Canada balsam, 107, 108
  - fleabane, 645
  - -hemp, 505
  - moonseed, 259
  - pitch, 108
  - snakeroot, 226
  - turpentine, 107
- Canadine, 595
- l-Canadine, 244
- *Canarium commune*, 389
- *Canavalia obtusifolia*, 341
- Canella, 440, 722
  - *alba*, 440
  - bark, 440
  - family, 439
- *Canellaceæ*, 439
- Canna, 133
  - *edulis*, 120
- ✓ Cannabis, 219, 221, 726
  - African, 221
  - Mexican, 219

Cannabis, Turkish, 221
  sativa, 219
Cantharides, 658
Cantharidin, 659
Cantharis vesicatoria, 658, 660
  vittata, 660
Caoutchouc, 401
Cape aloe, 156
  gum, 353
Caprifoliaceæ, 610
Capriola dactylon, 141
Caproic acid, 395
Caprylic acid, 394
Capsaicin, 570
Capsicum, 568, 728
  Indian, 571
  Japanese, 571
  Madras, 571
Capsicum annum, 571
   var. *canoides*, 568
   var. *longum*, 568
  frutescens, 568
Caragana pygmæa, 333
Caramel, 136
Caraway, 465, 726
  black, 466
  kümmel, 466
  Levant, 466
  Mogador, 466
  North Russian, 466
  oil, 466
  seed, 465
Carbohydrases, 690
Carbohydrates, 46
Carbolized gauze, 427
Carcharias limbatux, 664
  milberti, 664
  obscurus, 664
Cardamom, 182, 184
  Abyssinnian, 184
  bastard, 184
  Bengal, 184
  Cameroon, 184
  Ceylon, 184
  East African, 184
  fruit, 183
  husk, 183
  Javanese, 184
  Madagascar, 184
  Nepal, 184
  oil, 183
  seed, 182, 723
  Siam, 184
  Siamese, 184
Cardol, 406
Carica papaya, 443
Caricaceæ, 443
Carmine, 657
  red, 656
Carminic acid, 656
Carnauba wax, 148, 661
  carnivora, 682
Carob bean, 609
Carolina vanilla, 343
  pink, 499
α-Carotene, 665
β-Carotene, 665
γ-Carotene, 665
Carotene in oil, 677
  with vitamin D concentrate in oil, 677
Carotenoids, 665
Carrageen, 84
Carron oil, 364
Carrot family, 459
  fruit, 471
Cartagena ipecac, 604
Carthamus, 174
  tinctorius, 174
Carum carvi, 465, 466
  copticum, 535
Carvacrol, 535
Carvone, 366, 534
Cascara amarga, 344, 722
  sagrada, 411, 416, 721, 722
Cascarilla bark, 401
Casein, 687
Casimiroa edulis, 383
  seed, 383
Cassava, 133
  starch, 120, 402
Cassia acutifolia, 344, 345, 347
  angustifolia, 345, 347
  buds, 276
  cinnamon, 271
  fistula, 353
   pulp, 353
  fœtida, 609
  holosericea, 347
  lignea, 273
  marilandica, 347
  obovata, 347
  occidentalis, 609
  oil, 271, 274
  purging, 353
Cassie oil, 329
Castanea, 726
  crenata, 216
  dentata, 216
  pumila, 216
  sativa, 216
Castilla elastica, 219
Castor, 682
  fiber, 682
  oil, 396
  -oil cake, 396
   seed, 396
Castoreum, 682
Castoridæ, 682
Cataria, 540
Catechin, 608
Catechol, 336
Catechu, 358, 731
Catechutannic acid, 608
Cathartocarpus fistula, 353
Catmint, 540
Catnep, 540, 727
Catnip, 540
Caulophyllum, 725
  thalictroides, 256
Cayenne cinnamon, 276
  pepper, 568
Ceanothus americanus, 421
Ceara rubber, 401
Cedar, 113
  leaf oil, 114
  oil, 114
Cedarwood oil, 114
Celandine, 293
Celastraceæ, 407
Celery fruit, 468, 726
  oil, 468
  seed, 468
Cellulose, 426
Centaurea minor, 504
Centauria cyanus, 312
Centaurium, 726
Centaury, 504
  American, 504
Central American rubber, 401
   sarsaparilla, 164
Cephaëline, 604, 606
Cephaëline hydrochloride, 6
Cephælis acuminata, 603
  emetica, 607
  ipecacuanha, 603
Ceratin, 693
Ceratonia siliqua, 609
Cerebral hypophysis, 698
Cervidæ, 682
Cerevisiæ, 87
  fermentum, 86
Cetacea, 680
Cetaceum, 681
Cetraria, 93
  islandica, 93
Cetyl palmitate, 681
Cevadine, 596
Ceylon calumba, 259
  cardamom, 184
  cinnamon, 271, 274, 723
Chalk, prepared, 730
Chamælirium luteum, 170
Chamomile, 626
  English, 626
  German, 626
  Hungarian, 626
  Spanish, 626
  Roman, 626
  wild, 628
Chandana, 337
Charcoal, 693
  activated, 206
  animal, 693
  purified animal, 206
  wood charcoal, 206
Charlock, 300
Chaulmoogra, 439
  oil, 439
  seed, 439
Chaulmoogric acid, 439
Chavica officinarum, 200
Checker-berry, 480
Cheese, 687
Chelidonine, 293
Chelidonium, 293, 727
  majus, 293
Chemical evaluation of drugs, 44
Chemistry of drugs, 45
  of volatile oils, 523
Chenopodiaceæ, 233
Chenopodium, 233, 722, 724
  ambrosioides, 234
   var. *anthelminticum*, 233, 234, 235
  oil, 233
Cherry, 320, 321
  juice, 322
  laurel, 320
   water, 320
  sour, 321
  syrup, 322
  wild, 320
Chestnut extract, 216
  leaves, 216, 727
Chicle, 483
Chicory, 636
Chimaphila, 479, 726
  maculata, 480
  umbellata, 479
China root, 168
Chinese agar, 82
  anise, 263
  blistering-flies, 660
  cinnamon, 271
  colza, 302
  galls, 213, 406

Chinese ginseng, 459
  opium, 284
  star anise oil, 462
Chinquapin bark, 216
Chionanthus, 489, 724
  virginicus, 489
Chios turpentine, 405
Chirata, 503, 728
Chiratin, 503
Chloroform-colchicine, 155
Chlorogalum pomeridianum, 312
Chocolate, 430
  bitter, 430
  sweet, 430
Cholera vaccine, 69
    bacterial, 69
    prophylactic, 69
Cholesterin, 664, 686
Cholesterol, 686, 685
Cholic acid, 686
Choline, 674
Chondrin, 693
Chondrodendron tomentosum, 259, 495
Chondrus, 84
  crispus, 84, 85
Chordata, 652
Chorionic Follutein, N.N.R., 702
  gonadotropins, 702
  korotrin, N.N.R., 702
  pregnancy tests, 703
Christmas rose, 250
Chrysanthemum cinerariæfolium, 639
  coccineum, 639
  leucanthemum, 642
  Marschalli, 639, 641
  roseum, 639, 641
Chrysaphanolanthranol, 339
Chrysaphanolanthrone, 339
Chrysarobin, 339, 731
Chrysin, 311
Chrysœriodictyol, 520
Chrysophanic acid, 347, 414
Cichorium intybus, 636
Cicuta maculata, 470
Cimicifuga, 245, 725
  racemosa, 245
Cimicifugin, 247
Cinchona, 596, 724
  alkaloids, 600
  bark, 596
  calisaya, 596
  flava, 596
  ledgeriana, 596
  officinalis, 596, 600
  pale, 596
  pallida, 596, 600
  red, 596, 600
  rubra, 596
  succirubra, 596
  yellow, 596
Cinchonidine, 600
  sulfate, 600
Cinchonine, 601
  sulfate, 601
Cinchotannic acid, 600
Cineol, 449, 451
Cinnamein, 306, 338
Cinnamic acid, 306, 486
  aldehyde, 275
Cinnamaldehyde, 275
Cinnamon, Batavia, 271, 274
  Cassia, 271, 274
Cinnamon, Cayenne, 276
  Ceylon, 271, 274, 723
  Chinese, 271
  Fagot, 271
  Java, 271
  oil of, 271, 274
  Saigon, 271, 274, 723
  wild, 276
Cinnamomum aromaticum, 271
  burmanni, 271
  camphora, 276, 279
  cassia, 271, 276
  loureirii, 271, 276
  oliveri, 276
  pedatinervum, 276
  zeylanicum, 271, 276
Cinnamyl aldehyde, 275
  cinnamate, 305, 338
  -cocaine, 365, 366
Cissampelos pareira, 261
Cistaceæ, 438
Citrated caffeine, 434
Citric acid, 374
Citrin, 676
Citron, 376
Citronella bay oil, 456
  grass, 141
  oil, 142
Citrullol, 618
Citrullus colocynthis, 617
  vulgaris, 621
Citrus aurantifolia, 376
  aurantium, 371, 372, 373, 374
    var. *amara*, 373
    var. *bigarade*, 373
    var. *vulgaris*, 373
  bergamia, 376
  limon, 374, 375
  medica, 376
  paradisi, 376
  sinensis, 371, 372
Civet, 682
Civetta, 682
Cladonia rangiferina, 94
Clarified honey, 660
  wine, 422
Claviceps purpurea, 88
Clematis vitalba, 249
Clostridium tetani, 73
  bifermentans, 76
  histolyticum, 76
  œdematiens, 76
  perfringens, 75, 76
  septicum, 75, 76
Clove, 452, 726
  bark, 276
  fruit, 452
  mother of cloves, 452
  oil, 452
  stems, 452
Clubmoss family, 100
Clusia macrocarpa, 438
  rosea, 438
Cluytia similis, 398
Coca leaves, 364
    Huanuco, 364
    Javanese, 365
    Truxillo, 365
Cocaine, 365, 366, 594
  hydrochloride, 366
Cocarboxylase protein complex, 670
Coccidæ, 653
Coccoloba uvifera, 336
Cocculin, 262
Cocculus, 728
  indicus, 262
  villosus, 168
Coccus, 653
  cacti, 653
  ilicis, 653
Cochin ginger, 177
Cochineal, 653, 656
  Honduras, 656
  Madras, 656
  Teneriffe, 656
Cochlearia, 303
Cochlospermum gossypium, 434
Cocillana, 389, 722
Coconut, 146
  oil, 147
  palm, 146
  shells, 147
Cocos nucifera, 146, 147
Cod liver oil, 662, 677, 678
      non-destearinated, 663
Codamine, 287
Codeine, 287, 595
  phosphate, 287
  sulfate, 287
Cœlenterata, 651
Co-enzymes I and II, 671
Coffea arabica, 608
  liberica, 608
Coffee, 608, 728
  bean, 608
  decaffeinized, 609
  hulls, 609
  Mogdad, 609
  roasted, 608
  Sacca, 609
  seed, 608
  Sultan, 609
Coir, 147
Cola, 432
  ballayi, 433
  family, 429
  nitida, 432
Colchiceine, 154
Colchicine, 153, 154, 593
Colchicum, 153
  autumnale, 153
  corm, 153, 725
  seed, 153, 725
Coleoptera, 657
Collinsonia, 546
  canadensis, 546
Collinsonin, 546
Colocynth, 617, 728
  pulp, 617
Colocynthin, 617
Colombo, 258
Colophony, 109
Color of drugs, 38
Coltsfoot, 646
Colutea cruneta, 347
Colza seed, 301
Commercial origin of drugs, 24
Commiphora abyssinica, 387
  berryi, 389
  kataf, 389
  molmol, 387
a-Commiphoric acid, 388
b-Commiphoric acid, 388
g-Commiphoric acid, 388
Common dogwood, 476
  milkweed, 513
  thyme, 534
  wormwood, 643

Compositæ, 623
Composite family, 623
Compound jalap powder, 515
  licorice powder, 348
  rhubarb powder, 231
  senna powder, 348
Compressed yeast, 87
Concentrated oleovitamin A and D, U.S.P., 677
  tuberculin, 71
Condensed milk, 687
Condurangin, 513
Condurango, 511, 722, 723
Cone flower, 638
Conhydrine, 469
γ-Coniceine, 469
Coniferales, 102
Coniferin, 310
Conifers, 102
Coniferyl alcohol, 188, 310
Conii folia, 470
Coniine, 394, 461, 469
Conium, 468, 726
  juice, 470
  leaves, 470
  maculatum, 468, 470
Constituents of digitalis purpurea, 579
Convallaria, 162
  flowers, 162
  majalis, 162
  root, 162, 724
Convallotoxin, 313
Convolvulaceæ, 514
Convolvulin, 310
Convulvulus pandurata, 516
  scammonia, 517
Copaiba, 349
  African, 349
  balsam, 349
  coriacea, 349
  guyanensis, 349
  langsdorfii, 349
  Maracaibo, 349
  Maranham, 349
  officinalis, 349
  oil, 349
  Para, 349
  resin, 349
  Venezuela, 349
Copaifera, 349
Copal, 350
Copei, 349
Copernicia cerifera, 148, 396
Copperhead, 679
Copra, 147
  olein, 147
  stearin, 147
Coptine, 250
Coptis, 250, 725
  anemonæfolia, 250
  trifolia, 245, 250, 256
Coriander, 466, 726
  Bombay, 468
  Indian, 468
  oil, 468
Corianderseed, 466
Coriandrum sativum, 466, 468
Coriaria, 347
  myrtifolia, 347, 544
Cork, 211
Cornaceæ, 476
Cornicularia aculeata, 94
Corn, 133
  meal, 729
  oil, 137
Corn silk, 138
  smut, 91
  starch, 133, 729
Cornu cervi, 693
Cornus, 476, 722, 723
  circinata, 476
  florida, 476
  sericea, 476
Coronilla scorpioides, 342
Corpus luteus, 713
  luteum-progestin, 712, 713
Corticosterone, 708
Corydalis, 294, 721
Corynebacterium diphtheriæ, 72, 73
Coscinium fenestratum, 259
Cosotoxin, 328
Cotarnine, 595
  chloride, 287, 289
Coto bark, 281
    false, 281
    para, 281
    true, 281
Cotton, 425
  absorbent, 425
  American upland, 425
  purified, 425
  Sea Island, 425
  flowers, 429
  root bark, 429, 722
  -seed cake, 429
  seed oil, 427
Cotula, 628
Couch grass, 140
Coumarin, 310, 342
Coumarouna odorata, 342
  oppositifolia, 342
Cowhage, 358
Cow-parsnip, 470
Cow's milk, 687
Cracca, 347
Cranesbill, 361
Cream of tartar, 422
Creatinine, 689
Creeping thyme, 536
Creosote, 210
  bush, 371
  carbonate, 211
Creta præparata, 651
Cretan dittany, 536
Cretinism, 704, 705
Crinum, 162
Crocin, 172
Crocus, 172
  sativus, 172, 173
Crotalidæ, 679
Croton eluteria, 401
  gubouga, 398
  oil, 398
  tiglium, 398
Crowfoot, 249
  family, 238
Crown allspice, 455
  bark, 596
Cruciferæ, 294
Crude drugs, 17
  tartar, 422
  tuberculin, 71
Cryptocarya moschata, 266
  pretiosa, 281
Cryptopine, 287
Cryptoxanthine, 665
Cube root, 355
Cubeb, 193, 724
  -berries, 193
Cucumis malo, 621
Cucumis sativus, 621
Cucurbitaceæ, 616
Cucurbita legenaria, 621
  maxima, 621
  occidentalis, 621
  pepo, 620
Cudbear, 94, 95
Cultivation of drug plants, 55
Culver's root, 582
Cumin, 473
Cuminum cyminum, 473
Cupraloin test, 159
Cuprea bark, 600
Curaçao aloe, 156
Curare, 495
  alkaloids, 596
Curarine, 496
Curcuma, 181, 725
  longa, 181
  zedoaria, 181
Curled dock, 232
Cuskus root, 141
Cusparia bark, 383
Cusparine, 383
Cusso, 327
Cuttlefish bone, 652
Cyanin, 311, 312
Cycadaceæ, 102
Cycadales, 102
Cycads, 102
Cycas sp., 120
Cydonia vulgaris, 323
Cydonium, 323
Cymarin, 313, 506, 509
Cymene, 535
Cynips aciculata, 213
Cynodon dactylon, 649
Cynoglossus officinale, 521
Cypripedium, 189, 724
  acaule, 191
  arietinum, 191
  candidum, 191
  hirsutum, 191
  parviflorum, 189
  pubescens, 189
Cytisus purgans, 347
  scoparius, 341

D

Dactylis glomerata, 649
Dahlia, 188
Daisy fleabane, 645
Dakota mustard, 300
Dalmatian insect powder, 639
Damar, 351
Damiana, 441, 722, 723, 726
  family, 441
Dammar, 351
Dandelion root, 634
Daphne fruits, 447
  gnidium, 446, 447
  laureola, 446
  mezereum, 446, 447
Daphnia, 152
Daphnin, 310, 447
Daphnopsis schwartzii, 447
Date, 148
Datura arborea, 564
  fastuosa, var. *alba*, 555
  metel, 555
  stramonium, 561, 562, 563, 564
  tatula, 561, 562
Daucus carota, 471

Deacetyldigilanid, A, B and G, 579, 580
Deadly nightshade leaf, 547
  root, 547
Decaffeinized coffee, 609
Deer's tongue, 343
ehydrated alcohol, 137
Dehydro-emodinanthrone-monomethyl ether, 339
Delissea acuminata, 623
Delphinin, 312
Delphinine, 247, 596
Delphinium, 728
  ajacis, 247
  consolida, 247
  staphisagria, 247
  urceolatum, 248
Denarcotized opium, 285
Deodorized opium, 285
Deramacentroxenus rickettsii, 70
Derris elliptica, 355
  malaccensis, 355
  negrensis, 355
  root, 355
Desiccated suprarenal, U.S.P., N.F., 706
Desoxycorticosterone Acetate, U.S.P., 708
Destructive distillation, products of, 105
Devil's shoestring, 355
Dextrin, 126, 729
Dextrose, 134
iabetes insipidus, 699
  mellitus, 696
Diacetylmorphine, 287, 288
  hydrochloride, 287
  tannic acid, 215
Diagnostic diphtheria toxin, 72
Diastase, 138, 690
Diatoms, 80
Dibucaine hydrochloride, 369
Dicentra canadensis, 294
  cucullaria, 294
Dick test toxin, 72
Dicotyledoneæ, 193
Dicotyledons, 193
Dicypellium caryophyllatum, 276
Diethylstilbestrol, U.S.P., 711
Digitalic acid, 577
Digitalin, 313, 576, 577
Digitalis, 572, 727
  adulterants, 582
  ferruginea, 582
  grandiflora, 582
  lanata, 582
    constituents of, 580
  lutea, 582
  powdered, 582
  pulverata, 572
  purpurea, 579
    constituents of, 579
  seed, 577
  semina, 577
  Spanish, 582
  thapsi, 582
igitalis ferruginea, 582
  lanata, 313, 580, 582
  lutea, 582
  monstrosa, 582
  orientalis, 580
  purpurea, 572
  thapsi, 582
Digitalis aglycones, 686
  digitoxigenin, 313, 579, 580, 686
  glycosides, 578
Digitonin, 576, 579
Digitoxin, 313, 576, 579, 580, 585
Digoxin, 580
Dihydromorphinone hydrochloride, 287, 289
Dilaudid, 298
Dill fruit, 471
Diluted hydrocyanic acid, 319
1,3-Dimethylxanthine, 435
Dioscorea, 171, 172, 724
  alata, 172
  villosa, 171
Dioscoreaceæ, 171
Diosma succulenta, 378
Diosmin, 377, 378
Diosphenol, 378
Diospyros, 483
  virginiana, 483
Diothane hydrochloride, 368
Diphtheria anatoxin, 73
  antitoxin, 74
  toxoid, 73
Diplococcus pneumoniæ, 76
Dipnoi, 662
Dipterocarpus spp., 349
Disaccharides, 129
Distilled extract of witch hazel, 309
Dog grass, 140, 141
Dog-fennel, 634
Dogbane family, 505
Dog's bane, 505
Dogwood, 476
  common, 476
  family, 476
  round-leaved, 476
  swamp, 476
Dolichos, 358
Dorema ammoniacum, 474
Dover's powder, 285
Dracæna ambet, 147
Dracontium, 150
Dragon's blood, 147
Dried adrenal substance, 706
  blood, 689
    serum, 689
  diphtheria antitoxin, 74
  saccharated Iceland moss, 94
  tetanus antitoxin, 75
  Yeast, U.S.P., 87, 678
    tablets, 678
Drimys winteri, 264
Drisdol, 677
Drosera, 725, 728
  anglica, 303
  longifolia, 303
  rotundifolia, 303
Droseraceæ, 303
Drug markets, 25
  plants, cultivation of, 55
Drugs, chemistry of, 18, 45
  collection of, 19
  commerce in, 24
  drying of, 20
  evaluation of, 32
    biological, 43
    chemical, 44
    microscopical, 39
    organoleptic, 35
    physical, 45
Drugs, garbling of, 21
  harvesting, 19
  history of, 13
  identification of, 33
  microchemistry of, 13
  packaging of, 22, 25
  powdered, 717
  production of, 17
  purity of, 33
  quality of, 33
  storage and preservation, 22
  study of, 14
Dryobalanops camphora, 279
Dryopteris filix-mas, 97, 98, 99
  marginalis, 98
  spinulosa, 98
Dry wine, 422
  Yeast, U.S.P., 87, 678
Duboisia, 547, 565
  hopwoodi, 565
  leichardtii, 565
  myoporides, 564
Dulcamara, 565, 724
Dulcamarin, 566
Dulcitol, 134, 688
Dulcose, 134
Dwarf pine needle oil, 111
Dyer's madder, 609

E

EAST African cardamom, 184
    sandalwood oil, 223
  India rubber, 401
  Indian arrowroot, 185
    dill, 470
    myrrh, 389
    tamarind, 354
Eberthella typhosa, 69
Ecballium elaterium, 620
Ecgonine, 365, 366, 594
Echinacea, 728
Echinacea angustifolia, 638
  pallida, 638
Ecuadorian sarsaparilla, 164
Edible canna starch, 120
Egg, 680
  albumin, fresh, 680
  fresh, 680
  hen's, 680
  shell, 680
  yolk, fresh, 680
Egyptian henbane, 561
  opium, 284
Elæis guineensis, 147
Elastica, 401
Elaterin, 620
Elaterinum, 620, 731
Elaterium, 620
Elder, American, 614
  bark, 614
  berries, 615
  berry wine, 614
  European, 614
  flower water, 614
  flowers, 614
  leaves, 615
Elecampane, 636
Elemi, Manila, 389
Elettaria cardamomum, 182, 184
Ellagic acid, 215
Elm, 217, 723
  bark, 217
  family, 216

Embelia ribes, 198
Emetic root, 607
Emetine, 604, 606
  hydrochloride, 606
Emodin, 347, 414
Emodinanthrone-monomethyl ether, 339
Empetrum nigrum, 479
Emulsin, 314, 315, 690
Encephalitis vaccine, herpes "F" strain (formalin-killed), 68
  Japanese type B, 68
Endocrine products, 694
  chalones, 694
  definition, 694
  dried and powdered glands, 694
  ductless glands, 694
  exocrine functions, 694
  fresh glands, 694
  gland extracts, 694
  glandular activity, 695
  history, 694
  hormones, 694
  mixed glands, 694
  natural hormones, 694
  synthetic hormones, 694
Endotoxins, 71
English chamomile, 626
  serpentary, 233
Entada scandens, 341
Enteric vaccine. 68
Enzymes, 50, 690
  amylolytic or carbohydrases, 690
    amylase, 690
    amylopsin, 690
    diastase, 690
    emulsin, 690
    invertase, 690
    malt diastase, 690
    maltase, 690
    myrosin, 690
    ptyalin, 690
    sucrase, 690
    zymase, 690
  esterases, 690
    lipase, 690
    pectase, 690
    urease, 690
  oxidizing, 690
    peroxidases, 690
    thrombin, 690
    zymase, 690
  proteolytic, 690
    erepsin, 690
    papain, 690
      peptidase I, 690
    pepsin, 690
    rennin, 690
    trypsin, 690
Ephedra, 116, 117
  equisetina, 116, 117
  helvetica, 116, 117
  sinica, 116, 117
  vulgaris, 116
Ephedrine, 117, 593
  hydrochloride, 118
  sulfate, 118
Epigæa repens, 479
Epinephrine, U.S.P., 707
  Hydrochloride Injection, U.S.P., 707
    Solution, U.S.P., 707
  Inhalation, U.S.P., 707
Epinephrine Injection, U.S.P., 707
  Solution, U.S.P., 707
  Suspension in Oil, N.N.R., 707
Epipremnum pinnatum, 150, 522
Equine encephalomyelitis vaccine, eastern strain and western strain, 68
Equisetales, 97
Equisetum, 97
Erepsin, 690
Ergocristine, 90
Ergonovine maleate, 90
Ergosine, 90
Ergosterol, 91, 667, 686
Ergot, 88, 729
  amines, 91
Ergotamine tartrate, 90
Ergotoxine, ethane sulfonate, 90
Ericaceæ, 476
Ericoideæ, 476
Ericolin, 478, 479
Erigeron canadense, 645
  heterophyllum, 645
  oil, 645
  philadelphicus, 645
Eriodictyon, 519, 722, 726
  californicum, 519
Ertron, 667
Eryngium yuccæfolium, 471
Eryngo, 471
Erythræa centaurium, 504
Erythrocentaurin, 504
Erythronium, 155
Erythronium americanum, 155
Erythrophlœum, 360
  guineense, 360
Erythroxylaceæ, 364
Erythroxylon coca, 364, 366
  novogranatense, 364
  truxillense, 364
Eserine salicylate, 341
  sulfate, 341
Espongia officinalis, 651
Esterases, 690
Estradiol, 686
Estradiol, U.S.P., 711
    a-Estradiol, 711
    b-Estradiol, 711
  Benzoate, U.S.P., 711
    propionate, 712
Estratriene, N.N.R., 711
Estriol, 686, 711
Estrogens, 710
  administration, 710, 711, 712
  amniotin, 711
  benzestrol, 711
  diethylstilbestrol, 711
  estradiol, 686, 711
    benzoate, 711
  estriol, 686, 711
  estrone, 686, 711
  function, 710
  hexesterol, 711
  hypoactivity, 710
  isolated or purified, 711
  premarin, 711
  preparations, 711
  therapeutic use, 711
Estrone, 686, 711
Ethanol, 137
Ethyl aminobenzoate, 370
Ethyl chaulmoograte, 439
Ethylmorphine hydrochloride 287, 288
Eucaine hydrochloride, 368
Eucalyptene (*d*-pinene), 449
Eucalyptol, 451
  (cineol), 449
Eucalyptus, 426, 449, 727
  amygdalina radiata, 450
  ficifolia, 450
  globulus, 449
  gunnii, 450, 488
  kino, 450
  leucoxylon, 450
  macrohyncha, 450
  obliqua, 450
  oil, 450
  piperata, 450
  resinifera, 450, 488
  rostrata, 450
  stellulata, 450
Eucarya spicata, 223
Eucatropine hydrochloride, 557
Eugenia caryophyllata, 452
  smithii, 359
Eugenol, 453, 454, 455
Eumycetes, 86
Euonymus, 722
  atropurpureus, 408
  europæus, 408
Eupatorin, 634
Eupatorium, 632, 727
  capillifolium, 634
  fœniculaceum, 634
  perfoliatum, 632, 634
  purpureum, 634
  teucrifolium, 634
Euphorbia, 399
  corollata, 399, 607
  ipecacuanha, 399, 607
  pilulifera, 399, 724
  resinifera, 399
Euphorbiaceæ, 393, 394
  secretory tissue, 393, 394
Euphorbium, 399
European arum, 150
  goat's rue, 358
  hellebore, 151
  huckleberry, 479
  mandrake, 551
  pennyroyal, 544
  skullcap, 543
Evernia prunastri, 94
Examination of powdered drugs, 717
Exanthematic typhus vaccine, 69
Exogonium purga, 514
Exotoxins, 72
Expressed almond oil, 318
Extract of beef, 688
  of licorice, 332
Extractum sanguis, 689
Extralin, N.N.R., 716

F

Factitious storax, 306
Fagaceæ, 209
Fagopyrum sagittalum, 120
Fagot cinnamon, 271
Fagus americana, 210
  sylvatica, 210
False coto bark, 281

False flax, 363
  pareira, 261
  sandalwood, 357
  unicorn, 170
Farfara, 646, 728
Fats, 48, 394
Fatty acids, formulas of, 395
Fenchone, 465
Fennel, 462, 726
  bitter, 462
  Macedonian, 465
  oil, 465
  Roman, 463
  sweet, 463
Fennelseed, 462
Fenugreek, 360, 728
Fer-de-lance venom solution, 72
Fermented milk, 687
Fermentum, Brewer's yeast, 86
  compressum, 87
Fertilizers, 64
Ferula assa-fœtida, 473
  fœtida, 473
  galbaniflua, 475
  sumbul, 473
Fever basil, 536
  root, 615
Ficus bengalensis, 222
  carica, 222
  elastica, 219, 401
  glomerata, 222
  religiosa, 222
  rumphii, 222
  sycomorus, 222
Fig, 222
  coffee, 222
Figwort family, 572
Fiji sandalwood oil, 223
Filicales, 97
Filicic acid, 98
Filicin, 98
Filmaron, 98
Fixed oils, 48, 394
Flacourtiaceæ, 438
Flake lac, 657
Flavones, 311
Flax family, 361
Flaxseed, 361
  meal, 364
  oil, 363
Fleabane, 645
  Canada, 645
  daisy, 645
  Philadelphia, 645
Flesh-colored asclepias, 513
Flesh-consuming family, 88
Floripondio datura, 564
Flour, 126
Fluavil, 483
Flückiger reaction, 130
Fœniculum dulce, 463
  piperitum, 463
  vulgare, 462, 463
Folia nicotianæ, 565
Folic acid, 675, 716
Follutein, 702
Foraminifera, 651
Foreign organic matter, 33
  inorganic matter, 33
Formosa oil of camphor, 279
Fortified wine, 422
Foxglove, 572
Fragaria chileonsis, 323
  vesca, 323
Fragaria virginiana, 323
Frangula, 416, 722
Frangula-emodin, 414
Frangulin, 312
Frankincense, 389
Fraxin, 310
Fraxinus, 490
Fraxinus americana, 490
  excelsior, 490
  ornus, 488
French berries, 419
  brandy, 421
  mustard, 302
  rose, 324
  turpentine oil, 109
  wormwood, 630
Fresh apple juice, 323
  egg, 680
Fringe tree bark, 489
Frostweed, 438
Frost-wort, 438
Fructosazone, 131
d-Fructose, 135
Fructus lappæ, 638
Fruit sugar, 135
Fucus, 82, 729
  nodosus, 82
  serratus, 82
  siliquosus, 82
  vesiculosus, 82
Fumariaceæ, 294
Fumitory family, 294

G

GADIDÆ family, 662
Gadoleic, 663
Gadus merluccius, 679
  morrhua, 662
Galactose, 134, 688
Galanga, 179, 729
Galangal, 179
Galbanum, 475
Galega, 358, 723, 726
Galega officinalis, 358
Galipea officinalis, 383
Galium circæzans, 333
  triflorum, 343
Gallic acid, 215
Gallotannic acid, 215
Gallus domesticus, 67, 680
Gambia kino, 336
Gambir, 607, 729, 731
Gamboge, 437, 730
  family, 437
Garcinia cola, 433
  collina, 438
  Hanburi, 437
  morella, 438
a-Garcinolic acid, 437
b-Garcinolic acid, 437
g-Garcinolic acid, 437
Garlic, 162
Gaultheria, 476, 480
  oil, 481
  procumbens, 480, 481
Gaultherin, 310
Gauze, 427
  absorbent, 427
  adhesive, 427
    absorbent, 427
  bandage, 427
  carbolized, 427
  iodoform, 427
  non-sterilized absorbent, 427
Gauze, plain, 427
  roller bandage, 427
  sterile absorbent, 427
Gelatin, 693
Gelidium cartilagineum, 82
Gelsemidine, 497
Gelsemine, 497, 498
Gelsemium, 496, 723
  sempervirens, 496
Gelsemoidine, 497
Genista tinctoria, 311
Gentiamarin, 503
Gentian, 501, 728
  American, 503
  blue, 503
  family, 501
  root, 501
Gentiana Andrewsii, 503
  Catasbæi, 503
  lutea, 501
  pannonica, 503
  puberula, 503
  punctata, 503
  purpurea, 503
  saponaria, 503
Gentianaceæ, 501
Gentianose, 503
Gentiin, 503
Gentiopicrin, 502, 503
Gentisin, 503
Geographical source of drugs, 17
Geraniaceæ, 361
Geranium, 361, 722
  family, 361
  maculatum, 361
German chamomile, 626
  mustard, 302
  pellitory, 643
  spearmint oil, 534
Geum, 328
  rivale, 328
Ghatti gum, 353
Gigartina mamillosa, 84, 85
Gillenia, 607
Gillenia stipulata, 607
  trifoliata, 607
Gilleniæ trifoliatæ radix, 607
Ginger, 177, 724
  African, 177
  Calcutta, 177
  Calicut, 177
  Cochin, 177
  family, 176
  Jamaica, 177
  Japanese, 177
  Martinique, 177
Gingerol, 179
Ginglymostoma cirratum, 664
Ginkgoales, 102
Ginkgo biloba, 102
Ginseng, 459
  Chinese, 459
  family, 456
  Japanese, 459
  Korean, 459
  radix, 459
Gitaligenin, 579
Gitalin, 576, 577
Gitoxigenin, 579, 580
Gitoxin, 579, 580
Gladiolus, 172
Glandulæ rottleræ, 399
Globin insulin with zinc, 698
Gluconapin, 312
Gluco-resins, 104

Glucosazone, 131
Glucose, 134
d-Glucose, 134
Glue, 693
Gluten, 126
Glycerinated vaccine virus, 67
Glycine, 688
  soja, 357, 358
Glycocholic acid, 686
Glycocoll, 688
Glycosides, 46, 309
  acid group, 310
  alcohol group, 310
  aldehyde group, 310
  anthraquinone group, 312
  cardiac group, 313
  cyanophore group, 312
  digitalis, 578
  oxy-coumarin group, 310
  phenol group, 309
  saponins, 312
Glycyramarin, 332
Glychrrhiza, 329
  ammoniated, 332
  extract, 332
  Russian, 723
  Spanish, 723
Glycyrrhiza glabra, 329
    var. *glandulifera*, 329, 330
    var. *typica*, 330
  lepidota, 333
  uralensis, 333
Glycyrrhizin, 331
  ammoniated, 332
Gnetales, 102, 116
Gnida polycephala, 310
Gnostopine, 287
Goa powder, 339
Goanese ipecac, 607
Goiter, 704
  exophthalmic, 705
  simple, 704
Golden seal, 242
  senecio, 646
Goldthread, 250
Gonads, 709
  definition, 709
  development, 709
  hormones, 709
Goosefoot family, 233
Gossypium barbadense, 425
  hirsutum, 425, 427, 428, 429
Grains of paradise, 184
Gramineæ, 119
Granati, 447
  cortex, 447
    fructus, 447
    radicis, 447
Granatum, 474
Granulated opium, 285
Grapefruit, 376
Grass family, 119
Gravel-root, 634
Greasewood, 371
Grecian foxglove, 582
Greek sage, 539
Green almond, 406
  hellebore, 150
  tea, 435
Gregory's powder, 231
Grindelia, 630, 736
  camporum, 630
  glutinosa, 632
  hirsutula, 632
  humilis, 630
  robusta, 630
Grindelia, squarrosa, 630
Grindeline, 631
Grindelol, 631
Grits, 127
Guaiacinic acid, 370
Guaiacol, 211
  carbonate, 211
α-Guaiaconic acid, 370
β-Guaiaconic acid, 370
Guaiac resin, 370
  wood, 370
Guaiaretic acid, 370
Guajacum officinale, 370
  sanctum, 370
Guapi bark, 389
Guarana, 409, 729
Guarea Rusbyi, 389
Guayule rubber, 401
Guinea pepper, 199
Gum arabic, 351
  asafetida, 473
  Benjamin, 483
  Karaya, 434
  myrrh, 387
  opium, 282
  thus, 105
  tragacanth, 334
  turpentine, 105
Gummi plasticum, 482
Gum-resins, 48, 104
Gums, 333
Gurjum balsam, 349
Gutta, 483
  percha, 482
    family, 482
  pertscha, 482
Guttiferæ, 437
Gymnospermæ, 102
Gymnosperms, 102

H

Habenaria conopsea, 188
Habitat, 17
Hæmatoxylon, 727
  campechianum, 356
Hagenia abyssinica, 327
Hairy skullcap, 543
Halibut liver oil, 663
    capsules, 677
    U.S.P., 663, 677
Hamamelidaceæ, 304
Hamamelin, 308-309
Hamamelis, 306
  bark, 306
  leaf, 306
  virginiana, 306, 309
  water, 309
Hancornia speciosa, 401
Hardhack, 328
Hardwickia spp., 349
Hartshorn, 418, 693
Hay-fever, 647
Hay-fever pollens, 648
  composite pollens, 648
    grass pollens, 648
    other pollens, 648
    tree pollens, 648
Heart-leaved skullcap, 543
Heath family, 476
Heather, 479
Hedeoma, 544
  pulegioides, 544
Hedysarum americanum, 333
Helenin, 636
Helianthemum, 438
  canadense, 438
Helicin, 310
Helleborein, 250
Helleborus fœtidus, 251
Hellebrus niger, 250
Helonias, 170, 724
Hematein, 356
Hematoxylin, 356
Hematoxylon, 356
Hemidesmus indicus, 168
Hemiptera order, 653
Hemlock bark, 116
  pitch, 108
Hemp, 221
Hempseed, 221
Henbane, 559
  Egyptian, 561
  seed, 561
Hen's egg, 680
Hepatica, 249
  triloba, 249
Hepatpleurum venulosum, 459
Heracleum, 470
  lanatum, 470
Herba adonidis æstivalis, 250
Hercules club, 458
Heroin, 287, 288
Hesperidin, 309, 372
Heuchera, 304
  americana, 304
Hevea braziliensis, 401
Hexavitamin, U.S.P., 679
  capsules, 679
  tablets, 679
Hexesterol, N.N.R., 711
Hibiscus bancroftianus, 425
  rosa-sinensis, 425
Hickory nuts, 207
Hicoria ovata, 207
  pecan, 207
Hiera picra, 441
High-bush cranberry bark, 612
Hippoglossus hypoglossus, 663
Hirudin, 652
Hirudo decora, 651
  medicinalis, 651
  quinquestriata, 651
Histamine, 394
  acid phosphate, 91
  phosphate, 91
Histidine monohydrochloride, 91
Holocaine hydrochloride, 368
Homatropine hydrobromide, 556
  methylbromide, 556
Honduras bark, 344
  cochineal, 656
  sarsaparilla, 164
Honey, 660
  clarified, 660
  strained, 660
Honeysuckle family, 610
Hops, 221
Hordeum, 139
  vulgare, 120, 124, 138
Horehound, 543, 727
  black, 543
  water, 543
  white, 543
Hormones, 50
Horsemint, 536
  oil, 535
Horse nettle berries, 565

Horseradish root, 303
Hound's tongue, 521
Huanuco coca leaves, 364
Human immune globulin, 77
  measles immune serum, 77
  scarlet fever immune serum, 77
  serums and globulins, 77
Humulus, 221, 725
  lupulus, 221
Hundred-leaved rose, 326
Hungarian chamomile, 626
  paprika, 571
Hybanthus (*ionidium*) *ipecacuanha*, 607
Hydnocarpic acid, 439
Hydnocarpus anthelmintica, 439
  Wightiana, 439
Hydrangea, 304, 723
  arborescens, 304
Hydrangin, 304
Hydrastine, 243, 244, 595
  hydrochloride, 244
Hydrastis, 242, 724
  canadensis, 242, 256
Hydrocyanic acid, 319
  diluted, 319
Hydrophyllaceæ, 519
Hydroquinone, 478
Hydrous inulin, 637
  maltose, 136
  1-rhamnose, 135
  wool fat, 685
Hydroxyconiine, 469
Hydroxystearin sulfate, 397
Hymenoptera order, 660
Hyoscine, 555
  hydrobromide, 555
Hyoscyami semen, 561
Hyoscyamine, 554, 594
  bromate, 554
  hydrobromide, 554
  sulfate, 554
Hyoscyamus, 559, 725, 726, 727
  ablus, 561
  muticus, 561
  niger, 559
Hypocreaceæ, 88
Hypoprium brevirostris, 664
Hyssop skullcap, 543

I

Iceland moss, 93
  jelly, 94
Ichthyocolla, 679
Idain, 312
Identification key of powdered drugs, 719, 721, 731
Ignatia, 493, 728
Ilex paraguariensis, 436
  verticillata, 407
Illicium, 263
  anisatum, 263
  japonicum, 263
  religiosum, 263, 281
  verum, 263, 462
Immersion oil, 115
Immunogens, 70
Impure quinine sulfate, 602
India rubber, 401
Indican aconites, 241
  azadirach, 390
  bdellium, 389
Indican, capsicum, 571
  colza, 302
  coriander, 468
  corn starch, 120
  dill-seed, 466
  gum, 353
  hemp, 219
  ipecac, 607
  jalap, 516
  licorice, 333, 360
  opium, 284
  physic, 607
  safflower, 174
  sarsaparilla, 168
  tobacco, 621
  tori, 302
  turnip, 150
  valerian, 616
Influenza virus vaccine, types A and B, 68
Infusorial earth, 730
Inositol, 673
Insecta class, 652
Insect flowers, 639
  powder, 639
    Dalmatian, 639
    Persian, 641
Insects in drugs, 22
Inspection and analysis of drugs, 51
Insulin, 696
  hyperinsulinism, 696
  hypoinsulinism, 696
  injection, 697
  insulin reference standard, 696
  zinc insulin, 696
Inula, 636, 728
  britannica, 624
  conyza, 582
  Helenium, 636
Inulin, 634, 635, 637, 638
Invert sugar, 129
Invertase, 690
Invertebrata, 652
Iodine, 81
Iodoform gauze, 427
Ionidium, 607
Ipecac, 603, 724
  American, 607
  and opium powder, 285
  bastard, 607
  Brazilian, 603
  Cartagena, 604
  Goanese, 607
  Indian, 607
  Nicaragua, 603
  Panama, 603
  Rio, 603
  spurge, 399, 607
  stems, 604
  striated, 607
  undulated, 607
  white, 607
    ligneous, 607
Ipecacuanhic acid, 604
Ipomea, 516, 722, 723
  resin, 517
Ipomœa batatas, 516
  fistulosa, 516
  orizabensis, 516
  pandurata, 516
  purpurea, 516
  simulans, 516
Ipurganol, 515, 517
Iridaceæ, 172
Iridin, 175, 310
Iris, 172
  family, 172
  florentina, 174
  germanica, 174
  pallida, 174
  versicolor, 175, 723
  virginica, 175
Irish moss, 84
Isinglass, 679
Iso-cholesterol, 685
Isodulcite, 135
Isodulcitol, 135
Iso-emodin, 414
Isoeugenol, 188
Isopelletierine, 449
Isurus punctatus, 664

J

Jaborandi, 379
  Maraham, 379
  Paraguay, 379
  Pernambuco, 379
Jack-in-the-pulpit, 150
Jaffarabad aloe, 160
Jalap, 514, 722
  Brazilian, 515
  compound powder, 515
  Indian, 516
  orizaba, 516
  resin, 515
  root, 514
  Tampico, 516
  wild, 516
Jalapin, 310, 515, 517
Jamaica dogwood, 360
  ginger, 177
  kino, 336
  quassia, 384, 723
  sarsaparilla, 164
  simaruba, 386
Jamaican licorice, 333
Jamestown weed, 561
Japan wax, 661
Japanese aconites, 241
  agar, 82
  belladonna, 554
  capsicum, 571
  chillies, 569
  galls, 213
  ginger, 177
  ginseng, 459
  lacquer, 406
  menthol, 531
  mustard, 302
  peppermint oil, 529
  star anise, 263
  valerian, 616
Jateorrhiza palmata, 258
Jatropha curcas, 398
Java cinnamon, 271
Javanese cardamom, 184
  coca leaves, 365
Jeffersonia diphylla, 226
Jennerian vaccine, 67
Jequirity, 360
Jervine, 596
Jimson weed, 561
Joe-pye weed, 634
Juglandaceæ, 207
Juglans, 721, 722
  cinerea, 207
  regia, 207, 333
Juniper, 111, 727

Juniper berries, 111
  oil, 112
  tar, 113
  wood, 113
    oil, 113
Juniperus communis, 111, 112, 113
    var. *depressa*, 111, 112
  oxycedrus, 113
  sabina, 113, 114
  virginiana, 114

K

Kalmia, 476
Kamala, 399, 729
Karoo buchu, 378
Kava, 201, 725
Kayara gum, 434
Keratin, 693
Kermes, 657
Kesso root oil, 616
Key for identification of powders, 721
Kickxia africana, 509
  elastica, 401
Kidney bean starch, 120
Kien oil, 113
King's paprika, 572
Kino, 335, 336, 731
  African, 336
  Australian, 336, 450
  Bengal, 336
  Butea, 336
  Gambia, 336
  Jamaica, 336
  red, 336
Kinotannic acid, 336
Kola, 432, 729
Kolanuts, 432
Königspaprika, 572
Korean ginseng, 459
Korotrin, 702
Kosteletzyka pentaçarpa, 425
Kousso, 327
Krameria, 351, 723
  argentea, 351
  cistoides, 351
  ixina, 351
  lanceolata, 351
  payta, 351
  tomentosa, 351
  triandra, 351
  Texas, 351
Kümmel, 466
Kumyss, 687

L

Labiatæ, 522
Labrador tea, 479
Lac, 657
  fermentatum, 687
  flake, 657
  seed, 657
  stick, 657
Lacmus, 95
Lacqueblue, 95
Lactic acid, 688
    organisms, 77
Lactobacillus acidophilus, 77
  arabinosis, 672
  bulgaricus, 77
  casei, 675, 716
  lactisacidi, 77
Lactoflavin, U.S.P., 670, 678
Lactosazone, 131
Lactose, 134, 687, 730
Lactuca elongata, 647
  muralis, 647
  virosa, 647
Lactucarium, 647, 731
Lady fern, 98
  slipper root, 189
Lakshadia indica, 657
Laminaria, 81
  cloustonii, 81
  digitata, 81
Lanatoside, 313, 580
  A, 580
  B, 580
  C, 580
Lanolin, 685
Lanthopine, 287
Lappa, 637, 728
Larch agaric, 91
  bark, 116
  turpentine, 106
Lard, 692
  benzoinated, 692
  oil, 692
Large-flowering spurge, 399
Larix decidua, 116
  europæa, 106
Larkspur, 247
Larocaine hydrochloride, 369
Larrea tridentata, 371
Lasiosiphon eriocephalus, 447
  meissnerianus, 447
Laudanine, 287
Laudanosine, 267
Lauraceæ, 269
Laurel family, 269
Lauric, 395
Laurus cassia, 269, 271
  cinnamomum, 269, 271
  nobilis, 282
Lavandula, 536
  latifolia, 537
  officinalis, 536, 537
  spica, 536, 537
  vera, 536, 537
Lavender, 536
  flower oil, 537
  flowers, 536, 537
  oil, 536, 537
  spike oil, 537
Leaf tobacco, 565
Lecanora, 95
Ledum, 479
  palustre, 479
Leea speciosa, 351
Leeches, 651
  American, 651
  Australian, 651
  five-striped, 651
  gray, 651
  green, 651
  speckled, 651
Leguminosæ, 329
Leguminous starches, 729
Lemon, 374
  balm, 546
  juice, 374
  oil, 375
    methods of extraction, 375
    terpeneless, 375, 376
  peel, 374
Leopard's bane, 624
Leptandra, 582, 725
Levant caraway, 466
  wormseed, 629
Levulose, 135
Liatris, 343
Lichens, 93
Licorice, 332
  American, 333
  extract, 332
  Indian, 333
  Jamaican, 333
  Manchurian, 333
  root, 329
  wild, 333
Life root, 646
Light oil of camphor, 279
Lignum juniperi, 113
  vitæ, 370
Lilaceæ, 150
Lily family, 150
Lily-of-the-valley flowers, 162
  root, 162
Lime juice, 376
Limettin, 311
Limonene, 372, 375
Limonium carolinianum, 482
Linaceæ, 361
Linalool, 535
Linimentum calcis, 364
Linoleic, 395
Linolenic acid, 395, 663
Linseed, 361, 728
  meal, 364
  oil, 363
  raw oil, 363
Linum usitatissimum, 361
Lipase, 690, 692
Lippia dulcis, 522
  Mexicana, 522
  scaberrima, 522
Lippiol, 522
Liquid apiol, 470
  glucose, 134
  storax, 305
Liquidambar orientalis, 305
  styraciflua, 305
Liriodendron tulipifera, 264
Lithræa caustica, 406
Litmus, 94, 95
Litsea citrata, 194
  cubeba, 194
Liver extracts, oral, 714
    U.S.P., 714
  Injection, U.S.P., 715
  parenteral, 715
  Solution, U.S.P., 715
  with stomach, 716
Liver-stomach endocrines, 713
    function, 713
    hypoactivity, 713
    pernicious anemia, 713, 714
  preparations, 716
    Liver With Stomach, U.S.P., 716
Liverwort, 249
Lobelanidine, 623
Lobelanine, 623
Lobelia, 621, 623, 727
  blue, 623
  cardinalis, 623
  inflata, 621, 623
  nicotianæfolia, 623
  oil, 623
  red, 623
  seed, 623
  syphilitica, 623

Lobeline, 623
l-Lobeline, 623
Lobeline hydrochloride, 623
Loco-weed, 360
Locust bark, 360
Loganiaceæ. 490
Logwood, 356
Lonchocarpus chrysophyllus, 355
  nicou, 355
  utilis, 355
Long buchu, 378
  nutmeg, 266
  pepper, 200
Lophophora spp., 446
Lota maculosa, 664
Louisiana long pepper, 568
  sport pepper, 568
Loxa bark, 596
Lumisterol, 667
Lungwort, 521
Lupinus albus, 188
Lupulin, 221, 729
Luteolin, 311
Lycopersicon esculentum, 566
Lycopodiaceæ, 100
Lycopodiales, 97, 100
Lycopodium, 100, 729
  annotinum, 101
  cernum, 101
  clavatum, 100, 101
  complanatum, 101
  inundatum, 101
  polytrichoides, 101
  rubrum, 101
  saururus, 101
  selago, 100
Lycopus, 543
  europæus, 543
  virginicus, 543

M

MACASSAR mace, 267
  nutmeg, 266
Mace, 266, 725
Macrotin, 247
Macrotomia cephalotes, 521
Macrotys, 245
Madagascar cardamom, 184
Madder, dyer's, 609
  family, 590
Madras capsicum, 571
  chillies, 569
  cochineal, 656
Magnesia, heavy, 730
  light, 730
Magnolia, 262
  family, 262
  glauca, 262
  Virginiana, 262
Magnoliaceæ, 262
Mahogany family, 389
Mahonia aquifolium, 254, 256
Ma-Huang, 116
Maidenhair fern, 98
Majorana hortensis, 544
Male fern, 97
  nutmeg, 266
Mallotus philippinensis, 399
Mallow family, 422
  leaves, 425, 726
Malt, 138
  diastase, 690
  extract, 138
Malt sugar, 136
Maltase, 690
Malted barley, 138
  milk, 687
Maltosazone, 131
Maltose, 134, 136
Malva folia, 425
  rotundifolia, 425
  sylvestris, 425
Malvaceæ, 422
Malvaviscus pentacarpus, 425
  mammalia, 680
Manaca, 568, 721
Manacine, 568
Manchurian licorice, 333
Mandelic acid, 319
    d-mandelic acid, 319
    l-mandelic acid, 319
    d-l-mandelic acid, 319
Mandelonitrile, 315, 320
  d-mandelonitrile, 315, 320
  l-mandelonitrile, 315, 320
  d-l-mandelonitrile, 315, 320
Mandragora, 551
  officinarum, 551
Mandrake, 252
Mangrove extract, 359
Manihot esculenta, 120
  glaziovii, 401
  palmata, 402
  utilissima, 402
Manila elemi, 389
Manna, 488
  sugar, 134, 135
Mannite, 135, 488, 489
Mannitol, 134, 135, 488, 489
Mannose, 487
Maple, 408
  black sugar, 409
  family, 408
  mountain, 409
  rock, 408
  silver, 409
  sugar, 408
  white, 409
Maracaibo copaiba, 349
Maranham copaiba, 349
  jaborandi, 379
Maranta, 133, 185
  arundinaceæ, 120, 185
  starch, 729
Marantaceæ, 184
Margosa, 390
Marigold, 628
Marihuana, 219
Marjoram, 544
  sweet, 544
  wild, 544
Marrubium, 543
  vulgare, 543
Marsdenia cundurango, 511
  erecta, 519
Marsh rosemary, 482
  skullcap, 543
  tea, 479
  trefoil, 504
Marshmallow flowers, 425
  leaves, 425
Marsh-mallow root, 422
Martinique ginger, 177
Masterwort, 470
Mastic, 403, 730
Mastich, 403
Maté, 436
Matico, 200, 727
Matricaria, 626, 726
Matricaria, *chamomilla*, 626
Mauritius vanilla, 187
Maw seed, 286
May apple, 252
Mayweed, 628
Measles convalescent serum, 77
  prophylactic serum, 77
Mecca senna, 347
Meconic acid, 284
Meconine, 287
Meconodine, 287
Medicago sativa, 360
Mel, 660
Melaleuca leucadendron, 452
Melia azedarach, 390
Meliaceæ, 389
Melilotin, 311
Melilotus, 343, 726
  altissima, 311
  officinalis, 343
Melissa, 546
  officinalis, 546
Meloidæ, 657
Menadione, 669, 678
  Bisulfite, U.S.P., 678
  injection, 678
  sodium bisulfite, 669, 678
    tablets, 678
Menaphthene, U.S.P., 678
Menapthone, 678
Meningitis serum, 76
Menispermaceæ, 257
Menispermum, 259
  canadense, 259
Mentha aquatica, 544
  arvensis, 534
  oil, 529
    piperascens, 529
    var. *canadensis*, 544
  piperita, 527, 528
  Pulegium, 544
  spicata, 533, 534
  viridis, 533, 534
Menthol, 529, 532
Menthone, 529
Menthyl acetate, 529
Menyanthes, 504
  trifoliata, 504
Mescal buttons, 446
Mesquite gum, 353
Metamucil, 590
Methanol, 210
b-Methyl-æsculetin, 549
Methyl alcohol, 210
  salicylate, 209, 481
Methyl-cephaëline, 606
b-Methylesculetin, 497, 515
Methylhydrocotoin, 414
2-Methyl-Naphthoquinine, U.S.P., 678
Methylpelletierine, 449
Methyltestosterone, U.S.P 710
Methysticum, 201
Metroxylon læva, 148
  rumphii, 148
  species, 120
Metycaine hydrochloride, 369
Mexican allspice, 454
  sarsaparilla, 164
  scammony, 516
  tea, 234
  valerian, 616
  vanilla, 187
Mezereon, 446

Mezereon family, 446
Mezereum, 446, 729
Microchemistry, 40
  of the balsams, 486
  of the sugars, 130
  of the volatile oil drugs, 527
Microscopic evaluation of drugs, 39
Microsublimation, 41
Middlings, 127
Milfoil, 645
Milk, 687
  buttermilk, 687
  condensed, 687
  cow's, 687
  fermented, 687
  malted, 687
  skimmed, 687
  sugar, 687
Milkweed, 513
  common, 513
  family, 511
  swamp, 513
Milkwort family, 390
Mimosaceæ, 329
Mint family, 522
Mints, 527
Minusops balata, 483
Mitchella, 608, 724
  repens, 608
Mixed enteric vaccine, 69
Mixtures of powdered drugs, 721
Moccasin venom, 72
Modified insulin, 698
Mogador caraway, 466
Mogdad coffee, 609
Molasses, 136
Molisch reaction, 130
Mollusca, 652
Monarda, 536
  didyma, 535, 536
    oil, 535
  fistulosa, 536
  oil, 536
  punctata, 535, 536
Monimia family, 269
Monimiaceæ, 269
Monkshood, 238
Monobromated camphor, 278
Monocotyledons, 119
Monosaccharides, 228
Monotropoideæ, 476
Montpellier scammony, 519
Moonseed family, 257
Moraceæ, 219
Morning glory, 516
    family, 514
Morphine, 287, 505
  acetate, 287
  hydrochloride, 287
  sulfate, 287
Moschidæ subfamily, 682
Moschus, 683
  moschiferus, 683
Mother of cloves, 452
Mother-of-thyme, 536
Mountain balm, 536
  maple, 614
Mucic acid test, 132
Mucilages, 333
Mucuna, 358, 729
  pruriens, 358
Mulberry family, 219
Mullein flowers, 586
  leaves, 585, 727
Mullein seed, 623
Mulu kilavarv, 389
Muroxide reaction, 434
Muscatel sage, 539
Musk, 683
  root, 473
Muskmelon, 621
Mustard, 298
  black, 295, 298
  brown, 298
  Dakota, 300
  family, 294
  French, 302
  German, 302
  flour, 302, 728
  Indian, 296
  Japanese, 297, 302
  oil, volatile, 303
  paste, 302
  prepared, 302
  sarepta, 296, 301
  Trieste, 296
  white, 298, 301
  wild, 300
  yellow, 297
Mutton suet, 684
Mycobacterium tuberculosis, 71 79
Mylabris, 660
  cichorii, 660
Myrcia oil, 456
Myrica, 206, 722, 723
  asplendifolia, 207
  carolinensis, 207
  cerifera, 206
  gale, 207
Myricaceæ, 206
Myricin, 691
Myristic acid, 395, 663
Myristica, 265
  argentea, 266, 267
  bicuhyba, 266
  fatua, 266
  fragrans, 266
  malabarica, 267
  officinalis, 266
  oil, 266
  sebifera, 266
  surinamensis, 266
Myristicaceæ, 264
Myrosin, 312, 314, 690
Myroxylon balsamum, 338
  pereiræ, 337
Myrrh, 387, 730
  African, 387
  Arabian, 387
  East Indian, 389
  family, 387
  gum, 387
  Somali, 387
  Yemen, 387
Myrtaceæ, 449
Myrtillin, 312
Myrtle family, 449
Myxedema, 704, 705

N

NARCEINE, 287, 290
Narcotine, 287, 290, 595
Naregamia alata, 607
Naringin, 372
Natal aloe, 160
National Formulary, 27, 31
Natural origin, 14
Natural Vitamin A in Oil, U.S.P., 676
Nearctic crotalideæ antivenin, 679
Neat's foot oil, 689
Nectandra, 261
  coto, 281
  Rodiæi, 261
Neen bark, 390
Neisseria intracellularis, 76
Nemathelminthes, 651
Neoprene, 401
Nepal cardamoms, 184
Nepeta cataria, 540
Neroli, 374
Nettle family, 222
Neurospora sitophilia, 674
New Jersey tea, 421
Ngai camphor, 279
Niacin, 671, 678
Niacinamide, 671, 678
Nicaragua ipecac, 603
Nicotiana persica, 565
  rustica, 565
  tabacum, 565
Nicotinamide, 671
  U.S.P., 678
    injection, 678
    tablets, 678
Nicotine, 565, 594
Nicotinic acid, 671
    Amide, U.S.P., 678
    U.S.P., 678
      tablets, 678
Nigella damascena, 466
  sativa, 466
  seed, 466
Night-blooming cereus, 445
Nightshade family, 546
Nitrogen-fixing bacteria, 77
Nitrous acid test, 159
Non-destearinated cod liver oil, 663, 677
Non-sterilized absorbent gauze, 427
Nopalea cochenillifer, 653
North American anti-snake-bite serum, 76
    antivenin, 679
  Russian caraway, 466
Northern prickly ash bark, 381
  xanthoxylum, 723
Notes on the key for identification of powdered drugs, 720
Novocaine hydrochloride, 369
Novatropine, 556
Nupercaine hydrochloride, 369
Nut shells, 728
Nutgall, 212, 722, 723
Nutmeg, 265, 725
  family, 264
Nutrose, 687
Nux vomica, 490, 728
  family, 490

O

OAT, 139
  starch, 120
Oatmeal, 139, 729
Ocimum viride, 536
Ocotea pseudo-coto, 281
Octofollin, N.N.R., 711

Odontaspis littocalis, 664
Odor of drugs, 38
Oenin, 312
Official drugs, 26, 31
    assays, 32
    definition, 31
    description, 31
    dose, 32
    synonyms, 31
    tests, 31
    title, 31
Oil, Burbot liver, 664
  cod liver, 663
  halibut liver, 663
  non-destearinated, 663
Oil of Ajowan, 535
  of allspice, 455
  of American wormseed, 233
  of angelica, 472
  of anise, 462
  of anthemis, 628
  of arbor vitæ, 114
  of bay, 456
  of bergamot, 376
  of betula, 481
  of birch tar, rectified, 209
  of bitter almond, 316
  of cade, 113
  of cajuput, 452
  of camphor, 279
  of Canada erigeron, 645
  of caraway, 466
  of cardamom, 183
  of cassia, 271, 274
  of chenopodium, 233
  of cinnamon, 271, 274
  of cloves, 452
  of copaiba, 349
  of coriander, 468
  of cubeb, 193
  of dwarf pine needles, 111
  of erigeron, 645
  of eucalyptus, 450
  of fennel, 465
  of flaxseed, 363
  of fleabane, 645
  of gaultheria, 481
  of Japanese valerian, 616
  of juniper, 111
  of lavender, 536
    flowers, 537
  of lemon, 375
  of mace, 267
  of myrcia, 456
  of myristica, 266
  of neroli, 374
  of nutmeg, 266
  of orange, 372
    flowers, 373
  of origanum, 545
  of pennyroyal, 544
  of peppermint, 528
  of pimenta, 455
  of rose, 224
  of rosemary, 537
  of rue, 378
  of Russian pennyroyal, 544
  of sambucus, 614
  of sandalwood, 223
    East African, 223
    Fiji, 223
    South Australian, 223
    West Australian, 223
    West Indian, 223
  of sassafras, 280
  of savin, 114
Oil of sesame, 587
  of spearmint, 534
  of spike lavender, 537
  of sweet almond, 318
    birch, 209, 481
    orange, 372
  of tar, 110
  of theobroma, 431
  of thuja, 114
  of thyme, 535
  of turpentine, 108
  of valerian, 616
  of wintergreen, 481
  of wormwood, 644
  percomorph liver, 664
  shark liver, 664
Oils, fixed, 48, 394
  volatile, 48, 105, 523
Old tuberculin, 71
Olea europæa, 487
Oleaceæ, 487
Oleic acid, 395, 663, 664, 685
Olein, 692
Oleoresins, 48, 104
  natural, 104
Oleovitamin A, U.S.P., 676
  A and D, U.S.P., 677
    concentrated, 677
    capsules, 677
  capsules, 677
  D, U.S.P., Synthetic, 677
Oleum cajuputi, 452
  erigerontis, 645
  gaultheriæ, 481
  hedeomæ, 544
  lavandulæ, 536
    florum, 537
  monardæ, 536
  origani, 545
  rusci, 209
  valerinæ, 616
Olibanum, 389
Olive family, 487
  oil, 487
  stone, 487
  sweet oil, 487
  wood, 487
Oliver bark, 276
Ononis spinosa, 333
Opaque bdellium, 389
Operculina turpethum, 516
Ophidia, 679
Opium, 282, 730
  alkaloids of, 287
  Chinese, 284
  denarcotized, 285
  deodorized, 285
  Egyptian, 284
  granulated, 285
  gum, 282
  Indian, 284
  Persian, 283
  powdered, 285
  Turkey, 283
Opopanax, 389
Opuntia coccinellifera, 653
Oral liver extracts, 714
Orange, 371
  berries, 373
  bitter oil, 373
    peel, 372
  flower oil, 374
    water, 374
  flowers, 373
  oil, 372
Orange oil, methods of extraction, 375
    terpeneless, 375, 376
  sweet oil, 372
    peel, 371
Orchid family, 185
Orchidaceæ, 185
Orchil, 94
Orchis coriophora, 188
  militaris, 188
  odoratissima, 188
  simia, 188
Orcinol, 95
Ordeal bean, 340
Oregon balsam, 107
  grape root, 254
Organioleptic evaluation of drugs, 35
Oriental cashew-nut, 406
Origanum, 545
  creticum, 536
  dictamnus, 536
  majorana, 544
  oil, 545
  vulgare, 545
Orinoco simaruba, 386
Orizaba jalap, 516
Orlean, 438
Orosul, 522
Orris, 174, 723
  root, 174
Orthoform-New, 370
Oryza sativa, 120, 139, 678
Os, 693
  sepiæ, 652
Osazones from date, 131
  from honey, 131
Osmunda claytoniana, 98
Ostrea virginiana, 652
Oswego tea, 536
Osyris tenuifolia, 223
Ortholithus regalis, 679
Otto of rose, 324
Ouabain, 313, 510
  G-strophanthin, 510
Ovarian Residue, N.F., 711
Ovary, N.F., 711
Ovis aries, 683, 684, 685
Ox bile, 686
    extract, 687
Oxalic acid, 212
Oxgall, 686
Oxidizing enzymes, 690
Oxytocin, 699
Oyster-shell, 652
  prepared, 652

P

PACKAGING of drugs, 22, 25
Palaquim spp., 482
Pale catechu, 607
  cinchona, 596
    Peruvian bark, 596
  rose, 326
Palembang benzoin, 486
Palicurea densiflora, 281
Palm oil, 147
Palmæ, 143
Palmitic acid, 395, 515, 663, 664, 684
Panama ipecac, 603
  rubber, 401
Panaquilon, 459
Panax fruticosum, 459

Panax ginseng, 459
  quinquefolium, 459
  repens, 459
Pancreas, 696
  islets of Langerhans, 696
Pancreatin, 692
Pansy, 442
Pantothenic acid, 672
Papain, 443, 690
  peptidase I, 690
Papaver, 285
  rhœas, 287
  somniferum, 282, 285, 286
    var, *album*, 282, 285
Papaveraceæ, 282
Papaverine, 289, 595
  hydrochloride, 287, 289
Papaw family, 443
Papilionaceæ, 329
Paprika, 571
  Hungarian, 571
  King's, 572
  rose, 571
  Spanish, 572
  Turkish, 571
Papua mace, 267
  nutmeg, 266
Para arrowroot, 402
  copaiba, 349
  sarsaparilla, 164, 168
Para-aminobenzoic acid, 674
Para-coto bark, 281
Paraguay jaborandi, 379
  tea, 436
Paramœcium, 651
Parathyroid Injection, U.S.P., 703
Parathyroids, 703
  active hormone, 703
  function, 703
  hyperfunction, 703
  hypofunction, 703
  preparations, 703
  uses, 703, 704
Pareira, 259, 724
Parenteral liver extracts, 715
Parostemine, 281
Parosteminine, 281
Parsley fruit, 470
  root, 470
Parsleyseed, 470
Parthenium argentatum, 401
Pasque flower, 249
Passiflora, 443, 726
  incarnata, 443
  lutea, 443
Passifloraceæ, 442
Passion flower family, 442
  vine, 443
Pasteur treatment, 67
Pasteurella pestis, 69
Paullinia cupana, 409
Payena spp., 482
Payta krameria, 351
Pea starch, 120
Peach kernel oil, 319
Peanut, 355
  butter, 355
  hay, 355
  oil, 355
    cake, 355
Pearl barley, 139
Pecan nut, 207
Pectase, 690
Pectin, 376
  sugar, 135
Pedaliaceæ, 586
Pelargonin, 312
Pelletierine, 449
  tannate, 447, 448
Pellitory, 643
  German, 643
Peltigera aphthosa, 94
Penang benzoin, 486
  rubber, 401
Penicillin, 78
  Neisseria, 78
  notatum, 78
Pennyroyal, 544, 727
  European, 544
  oil, 544
  Russian, 544
Pentadesma butyraceum, 433
Pentavalent gas gangrene antitoxin, 75
Peonin, 312
Peperomia acuminata, 200
Pepo, 728
Pepper, black, 195
  family, 193
  hull, 197
  red, 568
  shell, 199
  white, 199
Peppermint, 527, 727
  oil, 528
    American, 529
    English, 529
    Japanese, 531
Pepsin, 690, 691
  scale, 691
  spongy, 691
Peptone, 689
Percomorph liver oil, 664, 678
Percomorphi, 664
Periandra dulcis, 333
  mediterranea, 333
Pernambuco jaborandi, 379
Peroxidases, 690
Persian berries, 419
  insect powder, 641
  opium, 283
  tragacanth, 335
Persic oil, 319
Persimmon, 483
Peru balsam, 337
Peru-resinotannol cinnamate, 338
Peruvian balsam, 337
  bark, 596
Petroselinum sativum, 470
Peucedanum sowa, 466, 470
Phæophyceæ, 80
Pharmaceutical resins, 104
Pharmacognosy, analytical, 51
  definition of, 11
  history of, 11
  medical, 12
Phaseolus multiflorus, 360
  vulgaris, 120
Phasianidæ family, 679
Pheasant's eye, 249
Phellandrene, 465
Phenacaine hydrochloride, 368
Phenylhydrazine reactions, 130
Philadelphia fleabane, 645
Phleum pratense, 649
Phlobatannins, 215
Phlorhizin, 309
Phlox ovata, 500
Phœnix dactylifera, 148
Physeter macrocephalus, 681
Physeteridæ, 680
Physic nuts, 398
Physical evaluation of drugs, 45
Physostigma, 340
  cylindrospermum, 341
  venenosum, 340
Physostigmine, 595
  salicylate, 341
  sulfate, 341
Phytelephas, sp., 148
  macrocarpa, 609
Phytolacca, 235, 724
  americana, 235
  fruit, 236
Phytolaccaceæ, 235
Phytomelane, 636
Picea canadensis, 108
  excelsa, 108
  mariana, 108
  rubra, 108
Picræna quassioides, 386
Picrasma excelsa, 384, 385, 386
a-Picrasmin, 386
b-Picrasmin, 386
Picrocrocin, 172
Picropodophyllin, 254
Picrotoxin, 262
Pigment glycosides, 311
Pill-bearing spurge, 399
Pilocarpine, 380, 594
  hydrochloride, 380
  nitrate, 380
Pilocarpus, 379
  jaborandi, 379, 380
  microphyllus, 379, 380
  pinnatifolia, 379
Pimenta, 454
  acris, 455
    var. *citrifolia*, 456
  officinalis, 454, 455
  oil, 455
  racemosa, 456
Pimenton, 572
Pimiento, 572
Pimpernel, 462
Pimpinella, 462
  anisum, 460
  magna, 462
  saxifraga, 462
Pine needle oil, 111
  oil, 110
    emulsion concentrate, 111
  pollen, 729
  tar, 110
Pinene, 535
Pink root, 499, 498
Pinus mugo, 111
  nigra, 109
  palustris, 105, 109, 110
  pinaster, 105, 109
  pumilio, 111
  sylvestris, 105, 111, 113, 114
  strobus, 115
  tæda, 105
Piper, 194
  angustifolium, 200, 582
  betle, 145
  borbonese, 194
  clusii, 194
  cubeba, 193
    var. *Rinæ badak*, 194
  longum, 200

Piper, *methysticum*, 201
  nigrum, 195
  officinarum, 200
  pedicellosum, 194
  ribesoides, 194
  sumatranum, 194
  sylvaticum, 200
Piperaceæ, 103
Piperine, 196
Piperonal (heliotropin), 281
Pipsissewa, 479
Piptostegia pisonis, 515
Pisces, 662
Piscidia erythrina, 360
Pistachio nut, 406
Pistacia lentiscus, 403
  terebinthinus, 405
  vera, 406
Pisum sativum, 120
Pitch, 110
Pitocin, 699
  Ampuls, N.N.R., 700
Pitressin, 699
  Ampuls, N.N.R., 700
  Tannate in Oil, N.N.R., 700
Pituitary body, 698
    anterior lobe, 700
      functions, 700
      hyperfunction, 701
      hypofunction, 701
      preparations, 702
      therapeutic uses, 702
    hyperfunction, 699
    official preparations, 700
    posterior lobe, 698, 699
    therapeutic use, 699
Pituri, 565
Pix nigra, 110
Placental extract, 77
  bacterial vaccine, 69
  prophylactic vaccine, 69
  vaccine, 69
Plain gauze, 427
Plantaginaceæ, 587
Plantago, 587
  arenaria, 587
  indica, 587, 589
  ovata, 587, 589, 590
  psyllium, 587, 588, 590
  seed, 587
Plant disorders, 64
Plantain family, 587
  seed, 587
    Indian, 587
Platyhelminthes, 651
Pleurisy root, 513
Plum kernels, 318
Pneumatophorus diego, 664
Pneumonia serum, type specific, 76
Poa pratensis, 649
Poaya blanca, 393
Podophyllotoxin, 254
Podophyllum, 252, 722
  emodi, 254
  indicum, 254
  peltatum, 252, 254
  resin, 254
Poison dogwood, 405
  elder, 405
  hemlock, 468
  ivy, 405
  oak, 405
  sumac, 405
Poisonous fungi, 92
Poke berries, 236
Poke root, 235
Pokeweed family, 235
Pollinosis, 647
Polyadenia pipericarpa, 198
Polygala alba, 393
  angulata, 393
  rubella, 393
  senega, 391
Polygalaceæ, 390
Polygalic acid, 393
Polygonaceæ, 227
Polygonatum, 164
  commutatum, 164
Polygonum bistorta, 233
Polypodiaceæ, 97
Polypodium, 98
  family, 97
  vulgare, 98
Polyporus officinalis, 91, 92
Polyscias nodosa, 459
Pomegranate bark, 447, 722, 723
  family, 447
  fruit, 447
    rind, 447
  pelletierine tannate, 447
  root and stem bark, 447
    bark, 447
Pompona vanilla, 188
Pontocaine hydrochloride, 369
Poplar bark, 202
  bud, 203
Poppy capsules, 285
  family, 282
  seed, 286
    oil, 286
      cake, 286
Populin, 202, 310
Populus alba, 202
  balsamifera, 201, 203
  candicans, 201, 203
  nigra, 206
  tacamahacca, 203
Porifera, 651
Port wine, 421
Posterior lobe of pituitary body, 698, 699
  Pituitary, U.S.P., 700
    injection, 700
Potato, 133
  fly, 660
  starch, 120, 729
Potentilla tormentilla, 328
Powdered cocoa, 431
  defatted ergot, 88
  digitalis, 572
  drugs, 717
    adulteration, 721
    examination, 717
    identification key, 719, 721, 731
    mixtures, 721
    notes on the key, 720
    procedure for identification, 719
  opium, 285
  oxgall extract, 687
  Stomach, U.S.P., 715
Powder of aloes and canella, 441
Powders, key for the identification of, 721
Pregnancy tests, 702
Premarin, N.N.R., 711
Premna arborea, 150, 522
Prepared cacao, 430
Prepared chalk, 651
  ergot, 88
  mustard, 302
  oyster shell, 652
Preserved ginger, 177
Prickly ash bark, 381
      northern, 381
      southern, 381
    berries, 383
  elder, 458
Prinos, 407
  verticillatus, 407
Procaine borate, 369
  hydrochloride, 369
  nitrate, 369
  procedure for identification of powdered drugs, 719, 721–731
Progesterone, 709
  U.S.P., 713
Propagation of drugs, 55
Prosopis juliflora, 353
Protamine zinc-insulin injection, 698
Proteins, 49
Proteolytic enzymes, 690
Protocurarine, 496
Protojervine, 596
Protopine, 287
Protozoa, 651
Provitamins-A, 665
  -D, 666
Prulaurasin, 312, 320
Prunasin, 312
Prune, 323
  kernels, 318
  pulp, 323
Prunus amygdalus, 316, 318
  dulcis, 316
  armeniaca, 319
  cerasus, 321, 322
  domestica, 323
  laurocerasus, 320
  mahaleb, 343
  padus, 312
  persica, 319
  serotina, 320
Prussic acid, 319
Pseudomonus radicicola, 77
Pseudopelletierine, 449
Pseudotannins, 215
Pseudotsuga douglasii, 107
Psychotrine, 604, 606
Psyllium, 587
  blond, 587
  seed, 587
    French, 587
    Spanish, 587
Ptelea trifoliata, 408
Ptercoyglutamic acid, 675
Pteridium aquilinum, 98
Pteridophyta, 97
Pteridophytes, 97
Pterocarpus erinaceous, 336
  marsupium, 335, 336
  santalinus, 336, 337
Pulmonaria, 521
  officinalis, 521
Pulsatilla, 249, 728
Pulse family, 329
Pulvis sanguis, 689
Pumpkin family, 616
  seed, 620
Punica granatum, 447
Punicaceæ, 447
Purging cassia, 353

Purging nuts, 398
  root, 607
Purified animal charcoal, 206, 693
  antidiphtheric serum, 74
  antitetanic serum, 75
  cotton, 425
  infusorial earth, 80
  kieselguhr, 80
  protein derivative of tuberculin, 71
  siliceous earth, 80
  storax, 306
Purple stramonium, 562
Pyrethri flores, 639
Pyrethrin I, 642
  II, 642
Pyrethrine, 643
Pyrethrum, 639, 643
  flowers, 725
  root, 643
Pyridoxal, 673
Pyridoxamine, 673
Pyridoxine, 673, 678
Pyrocatechol, 608
Pyrogallic acid, 216
Pyrogallol, 216
Pyrogallotannins, 215
Pyrola maculata, 480
Pyroloideæ, 477
Pyrularia pubera, 222
Pyrus malus, 323

Q

Quassia, 384, 727
  amara, 384, 385, 386
  bark, 386
  cups, 385
  family, 384
  Jamaica, 384, 723
  Surinam, 384, 723
Quassin, 386
Quebrachine, 511
Quebracho, 511
  bark, 511
  blanco, 511
Queen's root, 398
Quercetrin, 311
Quercitron bark, 211
Quercus, 211
  alba, 211
  coccinea, 213
  imbricaria, 213
  infectoria, 212
  lobata, 213
  occidentalis, 211
  suber, 211
  tinctorius, 311
  velutina, 211
  virens, 213
Quillaja, 326, 722
  saponaria, 326
Quillajasapotoxin, 327
Quince seed, 323
  jelly, 324
Quinic acid, 600
Quinidine, 601
  sulfate, 601
Quinine, 601, 602
  acid sulphate, 602
  and urea hydrochloride, 602
  bisulfate, 602
  dihydrochloride, 602
  ethylcarbonate, 602
Quinine, equinine, 602
  glycerophosphate, 602
  hydrobromide, 602
  hydrochloride, 602
  hypophosphite, 602
  phosphate, 602
  salicylate, 602
  sulfate, 602
  tannate, 603
  valerate (valerinate), 603
Quinone, 600
Quinovin, 600
Quisqualis indica, 630

R

Rabies vaccine, 67
Racemic mandelic acid, 319
Radix ginseng, 459
  iwarancusæ, 141
  palmæ christi, 192
Ragwort, 646
Raisins, 421
  California, 421
  Corinthian, 421
  Italian, 421
  Malaga, 421
  Spanish, 421
  Sultana, 421
Ramona stachyoides, 279
Ranunculaceæ, 238, 256
Ranunculus bulbosus, 249
Rape seed, 301
Rasamala wood oil, 306
Raspberry, 322
  juice, 322
  syrup, 323
Rattlesnake, 679
Raw linseed oil, 363
Rectified birch tar oil, 209
  tar oil, 110
  turpentine oil, 109
Red algæ, 82
  bark, 596
  cedar, 114
  cinchona, 596
  clover blossoms, 344
  gum, 450
  Peruvian bark, 596
  raspberries, 322
  raspberry juice, 322
  root, 421
  rose, 324
  saunders, 336, 727
  squill, 162
  wines, 421
Reference standard posterior pituitary powder, 699
Refined tetanus toxoid, 73
Regaliz de Cuba, 522
Remijia pedunculata, 600
  purdieana, 600
Rennin, 690
Reptiles, 679
Reptilia class, 679
Reseda luteola, 311
Resenes, 104
Resin, 109
  acids, 103
  alcohols, 103
  damar, 351
Resina draconis, 147
  drastica, 515
  scammonii, 517
Resinols, 103
Resinotannols, 103
Resins, 48, 103
Rhamnaceæ, 410
Rhamnetin, 347
Rhamnose, 134, 135
Rhamnus californica, 412, 416
  carniolica, 417
  cathartica, 410, 418, 419, 726
    fruit, 418, 419
  frangula, 416, 417
  infectoria, 419
  purshiana, 411, 416
  saxatilis, 419
Rhapontic rhubarb, 232
Rhaponticin, 232
Rhatany, 351
Rheum officinale, 227
  palmatum, 227, 232
  rhaponticum, 227, 232
Rhizophora mangle, 359
  mucronata, 359
Rhododendron, 476, 479
Rhodophyceæ, 82
Rhubarb, 227, 722
Rhus diversiloba, 406
  fruits, 405
  galls, 405
  glabra, 405, 727
  japonica, 213, 406
  radicans, 405
  semilata, 213, 406
  succedanea, 406
  toxicodendron, 405, 406
  typhina, 405
  vernicifera, 406
  vernix, 405
Riboflavin, 670
  U.S.P., 678
    injection, 678
    tablets, 678
Rice bran, 139
    U.S.P., 678
  polishings, 139
    extract, 140
    U.S.P., 678
  starch, 120, 729
Richardia scabra, 607
Ricin, 396
Ricinoleic acid, 395, 396
Ricinus communis, 396
Rickettsiæ, 69
  prowazeki, 69
Rio ipecac, 603
Riodine, 398
Roasted coffee, 608
Robinia, 360
  pseudacacia, 333, 360
Rocella fuciformis, 94, 95
  tinctoria, 94, 95
Rockrose family, 438
Rocky Mountain spotted fever vaccine, 69
Rodentia, 682
Roller gauze bandage, 427
Roman chamomile, 626
  fennel, 463
Rosa alba, 326
  canina, 188, 326
  centifolia, 326
  damascena, 326
  Gallica, 324
Rosaceæ, 314, 315
Rosæ caninæ fructus, 326
Rose, 324
  attar of, 324
  family, 314

Rose, French, 324
  hips, 326
  hundred-leaved, 326
  oil, 324
  otto of, 324
  pale, 326
  paprika, 571
  red, 324
  stronger water, 326
  water, 326
Rosemarinus, 537
  officinalis, 537
Rosemary, 537
  leaves, 538
  oil, 537, 538
Rosenpaprika, 571
Rosin, 109, 730
Rotenone, 355
Rottlera, 399
Rottlerin, 400
Round-leaved dogwood, 476
Royal salep, 192
Rozsapaprika, 571
Rubber, 219, 401
  African, 401
  Assam, 219
  Bahia, 401
  Borneo, 401
  Ceara, 401
  Central America, 219, 401
  East India, 401
  Guayule, 401
  India, 401
  Panama, 401
  Penang, 401
  synthetic, 401
Rubia, 609
  tinctorum, 312, 609
Rubiaceæ, 590
Rubus, 323, 722
  idæus, 322
  nigrobaccus, 323
  occidentalis, 323
  strigosus, 322
  villosus, 323
Rue, 378
  family, 371
  oil of, 387
Ruellia, 499, 724
  ciliosa, 499
Rumex, 232
  Brittanica, 232
  crispus, 232, 721
  obtusifolius, 232, 722
Rusbyine, 390
Russian flies, 658
  glycyrrhiza, 723
  spearmint oil, 534
  sturgeon, 679
Rusty foxglove, 582
Ruta graveolens, 378
Rutaceæ, 371
Rutin, 378
Rye ergot, 88
  flour, 729
  middlings, 729
  starch, 120, 124, 729

S

Sabadilla, 153
Sabbatia, 504
  angularis, 504
Sabina, 113
Sacca coffee, 609
Saccharomyces cerevisiæ, 87, 674, 678
  siccum, 87
Saccharomycetaceæ, 86
Saccharum, 134, 136
  officinarum, 136
Safflower, 174
Saffron, American, 174
  Spanish, 172
Safrol, 281
Sage, 538, 727
  Greek, 539
  Muscatel, 539
  Sclary, 539
  Spanish, 539
Sago, 102, 133, 148, 729
  imitation, 729
  starch, 120
Saigon cinnamon, 271, 274, 723
  Ignatius bean, 493
St. Vincent arrowroot, 185
Salep, 191
Salicaceæ, 201
Salicin, 202, 310
Saligenin, 202, 310, 611
Salinigrin, 310
Salix, 201
  alba, 201
  discolor, 201, 202, 310
  fragilis, 202
  nigra, 202
  purpurea, 202
Salmonella paratyphi, 69
  schottmülleri, 69
Salvia, 538
  lavandulæfolia, 539
  officinalis, 538
  pratensis, 539
  triloba, 539
  Sclarea, 539, 582
Sambucus, 614
  canadensis, 614
  nigra, 312, 614
Sambunigrin, 312
Sandalwood family, 222
  oil, 223
Sandarac, 108, 730
Sanguinaria, 290, 725
  canadensis, 290
Sanguinarine, 291, 596
Sanguis, 689
  draconis, 147
Santal oil, 223
Santalaceæ, 222
Santalic acid, 337
Santalin, 337
Santalum album, 222, 223
  preissianum, 223
  yasi, 223
Santonica, 629, 630, 725
Santonin, 629, 630
Sapindaceæ, 409
Sapodilla gum, 483
Sapogenin, 312
Saponins, 686
Sapotaceæ, 482
Sapotoxin, 312
Sappan, 357
Sarcocolla, 335
Sarepta mustard, 301
Sarsaparilla, 164, 457, 724
  American, 457
  Central American, 164
  Ecuadorian, 164
  Honduras, 164
Sarsaparilla, Jamaica, 164
  Mexican, 164
  Para, 164, 168
  Virginian, 457
  wild, 457
Sarsapogenin, 313
Sassafras, 279, 724
  bark, 279
  oil, 280
  pith, 279
Sassafras albidum, 279, 280
  variifolium, 279
Sassy bark, 360
Savanilla rhatany, 351
Savin, 113
  oil, 114
Saw palmetto berries, 143
Saxifragaceæ, 304
Saxifrage family, 304
Scale pepsin, 691
Scammoniæ radix, 517
Scammonium, 517
Scammony, 517, 730
  Mexican, 516
  Montpellier, 519
  resin, 517
  root, 517
  virgin, 518
Scarlet fever antitoxin, 75
    convalescent serum, 77
    streptococcus antitoxin, 75
      toxin, 72
Scarlet runner bean, 360
Schick test toxin, 72
Schinsent, 459
Schinus molle, 404
Schizomycetes, 66
Schœnocaulon officinalis, 153
Schönteten's reaction, 159
Scilla bulbus P.I., 160
Scillaren A, 160, 313
  B, 160
Sclary sage, 539
Scoparius, 341, 725, 728
Scopola, 552
  leaf, 553
  rhizome, 551, 552
Scopoletin, 497, 517
Scopolamine, 553, 555, 561, 564
  hydrobromide, 555
Scopolia carniolica, 552, 553, 554
  japonica, 554
Scopolin, 311
Scotch pine needle oil, 111
Scrophulariaceæ, 572
Scutellaria, 540, 727
  altissima, 543
  canescens, 542, 543
  cordifolia, 543
  galericulata, 543
  integrifolia, 543
  lateriflora, 540, 542
  pilosa, 543
Scutellarin, 543
Secale cereale, 120, 124
  cornutum, 88
Seed lac, 657
Selenicereus grandiflorus, 445
Selenipedium chica, 188
Seliwanoff test, 132
Semecarpus anacardium, 406
Seneca snakeroot, 391
Senecio, 646, 728

Senecio, golden, 646
  jacobæa, 647
  vulgaris, 647
Senega, 391, 728
Senna, 344, 726, 727
  Aden, 347
  Alexandria, 344, 345
  Arabian, 347
  compound powder, 348
  leaves, 344
  Mecca, 347
  pods, 347
  Tinnevelly, 345
Sepia officinalis, 652
Serenoa, 143
  repens, 143
Serpentaria, 224, 725
Serum, antimeningococcic, 76
  antipneumococcic, 76
  measles, 77
  meningitis, 76
  pneumonia, 76
  scarlet fever, 77
Sesame family, 586
  leaves, 587
  oil, 587
  seed, 586
Sesamum, 586, 587
  indicum, 586, 587
  seed, 586
Seven barks, 304
Shark, 664
  black tip, 664
  dusky, 664
  lemon, 664
  leopard, 664
  liver oil, 664, 678
  makerel, 664
  nurse, 664
  sand, 664
  white, 664
Shellac, 657
Sherry wine, 421
Shikimmi, 263
Shorea Wiesneri, 351
Shorts, 127
Siabenzoresin benzoate, 485
Siam benzoin, 483
  cardamom, 184
Siaresinotannol benzoate, 485
Siberian pine needle oil, 111
Sida ovalis, 425
Siliceous earth, 80
Simaruba bark, 386
  Jamaica, 386
  Orinoco, 386
Simaruba amara, 386
  officinalis, 386
Simarubaceæ, 384
Sinalbin, 312
Sinapsis alba, 301
Sinigrin, 298, 300, 312
Skimmed milk, 687
Skimmi, 263
Skimmin, 264, 310
Skullcap, 540
  European, 543
  hairy, 543
  heart-leaved, 543
  hyssop, 543
  marsh, 543
  western, 543
Skunk cabbage, 150
Sleepy grass, 143
Slippery elm, 217
Smallpox vaccine, 67
Smilax, 164
  aristolochiæfolia, 164
  medica, 164
  officinalis, 164
  ornato, 164
  papyracea, 164, 168
  Regelii, 164
  sarsaparilla, 164
Snake venins, 72
Soap bark, 326
  tree bark, 326
Soapberry family, 409
Socotrine aloe, 156
Sodium alginate, 82
  ascorbate injection, 675, 679
  caseinate, 687
  eugenolate, 454
Soil, 63
  fertility, 63
  management, 64
  physical condition of, 63
  topography, 64
Solanaceæ, 546, 555
Solanaceous alkaloids, 554
Solanine, 568
Solanum, 565, 566, 724, 727
  carolinense, 565
  dulcamara, 566
  lycopersicum, 566
  Melongena, 566
  nigrum, 566
  tuberosum, 120, 565
Solenostemma argel, 347
Solomon's seal, 164
Somali myrrh, 387
Sorghum halepense, 649
Sour wine, 422
South American arrow poison, 495
South Australian sandalwood oil, 223
South Sea arrowroot, 172
    Island arrowroot, 185
Southern prickly ash bark, 381
  xanthoxylum, 723
Soy bean, cake, 357
    hay, 357
  meal, 358
  oil, 358
Spagnum, 96
Spanish chamomile, 626
  digitalis, 582
  flies, 658
  glycyrrhiza, 723
  hops, 536
  paprika, 572
  saffron, 172
  sage, 539
Sparkling wine, 422
Sparteine, 342
  sulfate, 341
Spartium junceum, 342
Spearmint, 533, 727
  oil, 534
    German, 534
    Russian, 534
Spermaceti, 681
Spermatophyta, 102
Spermatophytes, 102
Sphyrna zygæna, 664
Spigelia, 499, 725
  marilandica, 499
Spigeline, 499
Spignet, 456
Spike oil, 537
  lavender oil, 537
Spinach, 233
Spinacia oleracea, 233
Spiræa ulmaria, 188
Spirea, 328
  tomentosa, 328
"Spirits" of turpentine, 108
Spiritus frumenti, 137
  vini gallici, 421
    rectificatus, 137
    vitis, 421
Sponge, 651
  bathing, 651
  burnt, 651
  Mediterranean, 651
  sheep's wool, 651
  tents, 651
  Turkey, 651
  Zimocca, 651
Spongy pepsin, 691
Spotted wintergreen, 480
Spruce gum, 108
Spurge family, 393
Squaw vine, 608
Squill, 160, 727
Squirrel corn, 294
Squirting cucumber, 620
Staff tree family, 407
Staminate cola, 433
Staphisagria, 247
Star anise, 263, 728
  oil, 462
  grass, 168
Starch, 119, 120, 133
  barley, 120
  Bermuda arrowroot, 120
  buckwheat, 120
  cassava, 120
  chemistry of, 125
  corn, 133
  edible canna, 120
  Indian corn, 120
  kidney bean, 120
  oat, 120
  pea, 120
  potato, 120
  rice, 120
  rye, 120
  sago, 120
  sweet potato, 120
  wheat, 120, 133
Starches, 119, 729
Statice, 482
  Limonium var. *caroliniana*, 482
Steapsin, 692
Stearic acid, 395, 515, 663, 684
Stearin, 692
Sterculia gum, 434
  tragacantha, 434
  urens, 434
  villosa, 434
Sterculiaceæ, 429
Stereocaulon paschale, 94
Stereolepis gigas, 664
Sterile absorbent gauze, 427
Sterols, 50, 685
Stick lac, 657
Stilbestrol, U.S.P., 711
Stillingia, 398, 722
  sylvatica, 398
Still wine, 422
Stinging nettle, 222
Stipa vaseyi, 143

Stomach preparations, 715
  Powdered Stomach, U.S.P., 715
  Ventriculin, N.N.R., 716
Stoneroot, 546
Storax, 305
  American, 305
  Levant, 305
  liquid, 305
  purified, 306
  factitious, 306
α-Storesin, 305
β-Storesin, 305
Storesin cinnamate, 305
Strained honey, 660
Stramonii radix, 564
  semen, 563
Stramonium, 561, 727, 726
  purple, 562
  radix, 564
  root, 564
  seed, 563
Straw foxglove, 582
Strassburg turpentine, 107
Strawberries, 323
Strawberry syrup, 323
Streptococcus carlsbergensis, 673
  fæcalis, 673, 675
  lactis, 675
  scarlatinæ, 72
Streptomyces griseus, 79
Streptomycin, 79
Striated ipecac, 607
Stronger rose water, 326
Strophanthin, 313. 509, 510
  G-Strophanthin, 509
  K-Strophanthin, 509
Strophanthus, 507, 725
  brown, 509
  courmontii. 509
  gratus, 509, 510
  green, 509
  hispidus, 507, 509
  Kombe, 507, 509
  sarmentosus, 509
Strychnine, 491, 493, 494, 595
  glycerophosphate, 493
  nitrate, 493
  phosphate, 493
  sulfate, 493, 494
  valerate, 493
Strychnos Castelnæi, 495
  Crevauxii, 495
  Ignatii, 493
  nux vomica. 490
  toxifera, 495
Styracaceæ. 483
Styracin, 305
Styrax family, 483
  benzoin, 483, 484
  officinale, 305
  tonkinensis, 483, 484
Succory, 636
Succus conii, 470
Sucrase, 690
Sucrose, 134, 136, 730
Suet, beef, 684
  mutton, 684
  prepared, 684
Sugar, 136
Sugars, 134, 228
  microchemistry of, 130
Suidæ, 691
Suint, 685
Sulfated hydrogenated castor oil, 397
  oils, 397
Sulfonated oils, 397
Sulfur, precipitated, 730
  washed, 730
Sultan coffee, 609
Sumac berries, 405
  family, 403
Sumatra benzoin, 483
Sumbul, 473, 725
Sundew, 303
  family, 303
Suprarenal, 706
Suprarenalin, U.S.P., 707
Suprasterols, 667
Surgeon's agaric, 91
Surinam quassia, 384, 723
Sus scrofa var. *domesticus*, 691, 692, 715
Swamp dogwood, 476
  milkweed, 513
Sweet almond, 316
  chocolate, 430
  fennel, 463
  fern, 207
  flag, 148
  gale, 207
    family, 206
  marjoram, 544
  oil, 487
  orange peel, 371
  potato starch, 120
  scabious, 645
  vernal grass, 343
  wine, 422
Sweet-scented bed straw, 343
Sweetia panamensis, 344
Swertia chirayita, 503
Swietenia mahogoni, 359, 389
Swine family, 691
Sylvacrol, 399
Symplocarpus fœtidus, 150
Synthetic camphor, 276
  local anesthetics, 367
  Oleovitamin D, U.S.P., 677
  rubber, 401
    buna N, 401
    buna S, 401
    butadiene 1, 401
    neoprene, 401
Syrian tragacanth, 335

T

Tabasco chillies, 568
  pepper, 568
Tacca pinnatifida, 185
Tachysterol, 667
Tagetes patula, 628
Tahiti arrowroot, 185
Talc, 730
Tall larkspur, 248
Tallow tree, 433
Tamarind, 354
  East Indian, 354
  pulp, 354
  West Indian, 354
Tamarindus indica, 354
Tampico jalap, 516
Tanacetum, 645
  vulgare, 645
Tannic acid, 215
Tannin, 215
Tannins, 47, 213
Tannins, classification, 215
Tansy, 645, 727
Tapioca, 133, 403
Taraktogenos kurzii, 439
Taraxacum, 634, 728
  lævigatum, 634
  officinale, 628, 634
Tartaric acid, 422
Taste of drugs, 38
Taurocholic acid, 686
Tea, 435, 726
  black, 435
  family, 435
  green, 435
  Paraguay, 436
Teaberry, 480
Teel oil, 587
Teleostei, 662
Teneriffe cochineal, 656
Tephrosia apollinea, 347
  spp., 347
  toxicaria, 355
  virginiana, 355
Terebene, 109
Terpeneless oils, 375
Terpin hydrate, 109
Terra alba, 730
Testa ovi, 680
Testosterone, 686
  pellets, 710
  Propionate, U.S.P., 709
Tetanus antitoxin, 75
  and gas gangrene antitoxin, 75
  toxoid, 73
Tetany, 703
Tetracaine hydrochloride, 369
Texas krameria, 351
  nutgalls, 213
  snakeroot, 224
Thalictrum flavum, 245
Thallophytes, 66
Thea sinensis, 435
    var. *bohea*, 435
    var. *viridis*, 435
Theaceæ, 435
Thebaine, 287, 290, 595
Theelin, U.S.P., 711
Theelol, N.N.R., 711
Theobroma, 429
  cacao, 429, 431
Theobromine, 431, 432
  and sodium acetate, 431
  and sodium salicylate, 431
Theocin, 435
Theophylline, 435
  and sodium acetate, 435
  ethylenediamine, 435
Thiamine hydrochloride, 670, 678
    U.S.P., 678
  injection, 678
  tablets, 678
  pyrophosphate, 670
Thoroughwort, 632
Thrombin, 690
Thuja, 114, 728
  occidentalis, 114
Thunnus thynnus, 664
Thyme, 534, 727
  oil, 535
Thymeleacea, 446
Thymol, 535
  iodide, 535
Thymus serpyllum, 536
  vulgaris, 534, 535

Thymus zygis, 535
  var. *gracilis*, 535
Thyroglobulin, 704
Thyroid gland, 704, 705
  function, 705
  hyperactivity, 705
  hypoactivity, 704, 705
  preparations, 705, 706
  therapeutic uses of, 705
  U.S.P., 705
Thyrotoxicosis, 705
Thyroxin, 704, 705
Tikitika, 139
  U.S.P., 678
Timbo root, 355
Tinnevelly senna, 345
Tinospora bakis, 259
Tobacco, 727
Tobasco, 454
α-Tocopherol, 667
b-Tocopherol, 667
g-Tocopherol, 667
Toddalia aculeata, 245
  lanceolata, 194
Tolu, 338
  balsam, 338
Tolu-resinotannol cinnamate, 339
Tonga, 150, 522, 721
Tonka, 342
  bean, 188
Tonquin beans, 342
Tormentilla, 328
Totaquine, 603
Toxicodendrol, 405
Toxisterol, 667
Toxin, diagnostic diphtheria, 72
  Dick test, 72
  scarlet fever, 72
  Schick test, 72
Toxins, 71
Toxoid, diphtheria, 73
  alum precipitated, 73
  tetanus, 73
Toxoids, 71, 72
Tragacanth, 334, 729
  gum, 334
  Persian, 335
  sorts, 334
  Syrian, 335
  veriform, 334
Tragopogon pratensis, 624
Trailing arbutus, 479
Transvaal croton bark, 398
Travesia sundaica, 459
Triakis semifasciatum, 664
Triasyn B Capsules, U.S.P. 679
  tablets, 679
Trifolium, 344, 726
  pratense, 344
Trigonella fænum-græcum, 360
Trilisa odoratissima, 343
Trillium, 171, 724
  erectum, 171
Triosteum, 615
  perfoliatum, 615
Triticum, 140, 728
  æstivum, 120, 124
Trivalent gas gangrene antitoxin, 75
Tropical American anti-snake bite serum, 76
  rattler anti-snake-bite serum, 76
True bittersweet, 565
  coto bark, 281
  cramp bark, 612
  fungi, 86
  palms, 143
α-Truxilline, 365, 366
β-Truxilline, 365, 366
Truxillo coca leaves, 365
Trypsin, 690, 692
Tsuga canadensis, 108, 116
Tuba root, 355
Tubera ari, 150
  salep, 191
Tuberculin-Koch, 71
Tuberculins, 71
  concentrated, 71
  crude, 71
  old, 71
  tuberculin-Koch, 71
Tulip-tree bark, 264
Turkey corn, 294
  opium, 283
Turkish cannabis, 221
  paprika, 571
Turmeric, 181
Turnera aphrodisiaca, 441
  diffusa, 441
Turneraceæ, 441
Turnip seed, 301
Turnsole, 95
Turpentine, 105
  oil, 108
Turpeth root, 516
Tussilago, 646
  farfara, 628, 646
Tutocaine hydrochloride, 368
Tylophora indica (*asthmatica*), 607
Typhoid and paratyphoid vaccine, 69
  bacterial vaccine, 68
  combined vaccine, 69
  prophylactic vaccine, 68
  vaccine, 68
Tyramine, 91
Tyrothricin, 80

U

UGANDA aloe, 160
Ulmaceæ, 216
Ulmus campestris, 218
  fulva, 217
Umbelliferæ, 459
Umbelliferon, 475
Umbelliferone, 310, 475
Uncaria gambir, 607
Undulated ipecac, 607
Urginea indica, 160
  maritima, 160, 161, 162
Unguiculata, 682
Ungulata, 682
Unicorn root, 168
Urease, 690
Urtica, 222
  dioica, 222
  urens, 222
Urticaceæ, 222
U. S. Pharmacopœia, 27, 31
Usnea barbata, 94
Ustilago, 91, 729
  zeæ, 91
Uva ursi, 477, 727

V

VACCINE, bacterial, 68
  cholera, 69
  encephalitis, 68
  equine encephalomyelitis, 68
  exanthematic typhus, 69
  influenza virus, 68
  plague, 69
  rabies, 67
  Rocky Mountain spotted fever, 69
  smallpox, 67
  typhoid, 68
    and paratyphoid, 69
  yellow fever, 67
Vaccines, 66
Vaccinioideæ, 476
Vaccinium myrtillus, 478, 479
  oxycoccus, 479
  vitis idæa, 479
Valerian, 615, 724
  family, 615
  Indian, 616
  Japanese, 616
  Mexican, 616
  oil, 616
Valeriana angustifolia, 616
  celtica, 616
  mexicana, 616
  officinalis, 615, 616
  sylvatica, 615
  wallichii, 616
Valerianaceæ, 615
Valerianic acid, 616
Valeric acid, 611, 616
Vanilla, 186, 187
  bean, 186
  Bourbon, 187
  Brazilian, 187
  cuts, 188
  grass, 343
  Mauritius, 187
  Mexican, 187
  planifolia, 186
  Pompona, 188
  tahitensis, 186
  splits, 188
  Venezuelan, 187
  Vera Cruz, 187
Vanillin, 188
Vanillons, 187
Vasopressin, 699
Vegetable ivory, 148
Venezuela copiaba, 349
  vanilla, 187
Venice turpentine, 106
Venins, 71, 72
Ventriculin, N.N.R., 716
Venus hair fern, 98
Vera Cruz vanilla, 187
Veratrine, 153
Veratrum album, 151
  viride, 150, 151, 152, 153
Verbasci flores, 586
  folia, 585
Verbascum phlomoides, 582, 586
  thapsiforme, 586
  thapsus, 585, 623
Verbena, 521
  hastata, 521
Verbenaceæ, 521
Vermiform tragacanth, 334
Veronicastrum virginicum, 582

- Veronica, 582
  - *virginica*, 582
- *Vertebrata*, 652
- Vervain family, 521
- Vetiver, 141
- *Vibrio comma*, 69
- Viburnin, 611
  - *dentatum*, 611
  - *lentago*, 611
  - *opulus*, 612, 722
    - var. *americanum*, 612
  - prunifolium, 610, 722, 723
    - *rufidulum*, 610
- Vine family, 421
- *Vinum*, 421
  - *album*, 421
  - *portense*, 421
  - *rubrum*, 421
  - *xericum*, 421
- Viola, 441
  - *odorata*, 442, 607
  - *pendata*, 441
  - *tricolor*, 442
- *Violaceæ*, 441
- Violet, 441
  - bird's foot, 441
  - family, 441
- Viosterol, 666
  - in Oil, U.S.P., 677
- Virgin scammony, 518
- Virginia snakeroot, 224
  - sarsaparilla, 457
- *Vismia laccifera*, 438
- *Vitaceæ*, 421
- Vitamin A, 663, 665
  - A_1, 665
  - A_2, 665
  - B complex, 669, 678
  - B_1, 670, 678
  - B_2, 670, 678
  - B_6, 673
  - B_c, 675
- Vitamin B_1 Hydrochloride, U.S.P., 678
  - C, 675, 679
  - D, 663, 666, 667
  - D_2, 666, 667
  - D_3, 666, 667
  - D_6, 678
- Vitamin E, 127, 667, 668
  - G, 670, 678
  - H, 672
  - K, 668, 678
  - K_1, 668, 669
  - K_2, 668, 669
  - M, 675
  - P, 676
- Vitamins, 50, 664
  - classification, 665–676
  - definition, 664
  - preparations, 676–679
- Vitellus, 680
- *Vitis sessilifolia*, 343
  - *vinifera*, 421
- *Viverra civetta*, 682
  - *zibetha*, 682
- Viverridæ family, 682
- *Viviania esculenta*, 347
- Volatile oils, 48, 105, 523
  - chemistry of, 523
  - classification, 523
    - alcohol group, 525
    - aldehyde group, 525
    - ester group, 527
    - hydrocarbon group, 524
    - ketone group, 525
- Volatile oils, classification, lactone and oxide group, 526
    - phenol group, 526
    - phenolic ether group, 526
  - drugs, microchemistry of, 527
  - of mustard, 303
- *Vorticella*, 651

W

- Wafer ash bark, 408
- Wahoo bark, 408
- Walnut family, 207
- Warburg's yellow enzyme, 671
- Water avens, 328
  - hemlock, 470
  - horehound, 543
  - mint, 544
  - moccasin, 679
- Waterleaf family, 519
- Watermelon, 621
- Wattle gum, 353
- Wax, 661
  - beeswax, 661
  - bleached, 661
  - carnauba, 661
  - Japan, 661
  - myrtle bark, 206
  - white, 661
  - yellow, 661
- Waxes, 48, 394, 395
- Waythorn, 418
- West Australian sandalwood oil, 223
  - Indian cashew, 406
    - sandalwood oil, 223
    - snake root, 344
    - tamarind, 354
- Western skullcap, 543
- Whale oil, 682
  - sperm, 681
- Whalebone, 682
- Wheat, 133
  - flour, 729
  - middlings, 729
  - starch, 120, 124, 133, 729
- Whey, 687
- White agaric, 91
  - ash bark, 490
  - cedar, 114
  - cinnamon, 440
  - gall, 213
  - hellebore, 151
  - horehound, 543
  - ipecac, 393, 607
  - ligneous ipecac, 607
  - mustard, 301, 728
  - oak bark, 211, 721, 722
  - oil of camphor, 279
  - pareira, 261
  - pepper, 199
  - pine, 115, 723
  - sandalwood, 222
  - senega, 393
  - wax, 661
  - wine, 421
- Whiskey, 137
- Whole Pituitary, N.F., 700
- Wild bergamot, 536
  - arrotseed, 471
  - chamomile, 628
  - cherry, 320, 721, 722
- Wild cherry, bark, 320
    - fruit, 320
    - wine, 320
  - cinnamon, 276
  - ginger, 226
  - horehound, 634
  - indigo root, 358
  - jalap, 516
  - lettuce, 647
  - licorice, 333, 360
  - liquorice seed, 360
  - mace, 267
  - marjoram, 545
  - mint, 544
  - mustard, 300
  - nutmeg, 266
  - passion flower, 443
  - potato, 516
  - sarsaparilla, 457
  - thyme, 536
  - yam root, 171
- Willow bark, 201
  - family, 201
- Wine, 421
  - brandy, 421, 422
  - clarified, 422
  - dry, 422
  - fortified, 422
  - French brandy, 421
  - port, 421
  - red, 421
  - sherry, 421
  - sparkling, 422
  - sour, 422
  - spiritus vini gallici, 421
  - spiritus vini vitis, 421
  - still, 422
  - sweet, 422
  - white, 421
- Winter squash, 621
- Wintera, 264
- Winterberry, 407
- Wintergreen, 480
  - oil, 481
- Winter's bark, 264
- Witch hazel, 306
  - bark, 306
  - distilled extract, 309
  - family, 304
  - leaves, 306, 727
- Wood alcohol, 210
  - charcoal, 206
  - creosote, 210
  - sugar, 135
  - tar, 210
- Wool fat, 685
- Wormwood, common, 643
  - French, 630
  - oil, 644

X

- *Xanthium macrocarpum*, 563
- Xanthorrhiza, 250. *See* Zanthorrhiza.
- Xantholine, 287
- Xanthoeriodictyol, 520
- Xanthones, 311
- Xanthoxylum, 381
  - fruit, 383, 728
  - northern, 723
  - southern, 723
- *Xiphias gladius*, 664
- *Xylopia*, 198
  - *aromatica*, 199
  - *frutescens*, 199

Xylopia grandiflora, 199
  æthiopica, 198
  sericea, 199
Xylose, 134, 135
l-Xylose, 135

Y

Yam, 172
  family, 171
Yarrow, 645
Yeast, 86
  family, 86
Yellow adder's tongue, 155
  bark, 596
  cinchona, 596
  dextrin, 126
  dock, 232
Yellow fever vaccine, 67
  jasmine root, 496
  melilotus, 343
  pareira, 261
  sweet clover, 343
  wax, 661
Yellow-root, 250
Yemen myrrh, 387
Yerba santa, 519

Z

Zanthorrhiza, 250
  apiifolia, 245, 250, 256
Zanthoxylum americanum, 381, 383
  clava-herculis, 381, 383
Zanzibar aloe, 160
Zapote blanco, 384
Zea, 138
  Mays, 91, 120, 127, 133, 137, 138
    everta, 127
    indentata, 127
    indurata, 127
    other varieties of, 127
    saccharata, 127
Zedoaria, 181
Zedoary, 181, 724
Zieria, spp., 245
Zingiber mioga, 177
  officinale, 177
  zerumbet, 177
Zingiberaceæ, 176
Zygophyllaceæ, 370
Zymase, 690

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